B186

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C12N 15/12, C07K 14/47, A61K 38/17, G01N 33/68, 33/573, C12N 1/21

A2

(11) International Publication Number: WO 95/21252

(43) International Publication Date: 10 August 1995 (10.08.95)

(21) International Application Number: PCT/US95/01210

(22) International Filing Date: 31 January 1995 (31.01.95)

(30) Priority Data:
08/190,802 1 February 1994 (01.02.94) US

(71) Applicant: THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY [US/US]; Office of Technology Licensing, Suite 350, 900 Welch Road, Palo Alto, CA 94304 (US).

(72) Inventors: MOCHLY-ROSEN, Daria; 325 Harvard Avenue, Menlo Park, CA 94025 (US). RON, Dorit; 840 Alvarado Street, San Francisco, CA 94114 (US).

(74) Agents: MURASHIGE, Kate, H. et al.; Morrison & Foerster, 2000 Pennsylvania Avenue, N.W., Washington, DC 20006 (US).

(81) Designated States: AU, CA, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
Without international search report and to be republished upon receipt of that report.

(54) Title: WD-40-DERIVED PEPTIDES AND USES THEREOF

(57) Abstract

The present invention relates to a polypeptide composition effective to alter the activity of a first protein that interacts with a second protein, where the second protein contains at least one WD-40 region. The polypeptides of the present invention typically have between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein. The invention further includes a method of altering the activity of the above described first protein. In one embodiment of the invention the polypeptide composition is effective to alter the activity of a protein kinase C, where the protein kinase C interacts with a second protein, and the second protein contains at least one WD-40 region (e.g., RACK1).

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

METHODS AND COMPOSITIONS FOR MODULATION OF VESICULAR RELEASE

This work was supported in part by NIMH Grant 5R37MH38710 and NIH Grant 2P50MH48108. Accordingly, the United States Government has certain rights in this invention.

Field of the Invention

The present invention relates to methods of identifying compounds capable of modulating vesicular release. In particular, the invention relates to (i) methods of identifying such compounds employing the secretion associated 17S (SA-17S) complex, and (ii) the proteins comprising the SA-17S complex.

References

Aalto, M.K., *et al.*, *EMBO J.* 12:4095-4104 (1993).

Ausubel, F.M., *et al.*, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, John Wiley and Sons, Inc., Media, PA (1992).

Bennett, M.K., *et al.*, *J. Cell. Biol.* 116:761-775 (1992).

Bennett, M.K., *et al.*, *Cell* 74:863-873 (1993).

Bowser, R., *et al.*, *J. Cell Biol.* 118:1041-1056 (1992).

Brennwald, P., and Novick, P., *Nature* 362560-563 (1993).

Buckley, K., and Kelly, R.B., *J. Cell Biol.* 100:1284-1294 (1985).

Elferink, L.A., *et al.*, *Cell* 72:153 (1993).

Harlow, E., *et al.*, ANTIBODIES: A LABORATORY MANUAL, Cold Spring Harbor Laboratory Press (1988).

Lane, R.D., *et al.*, *Meth. Enzymol.* 121:183-192 (1986).

Malgaroli, A., and Tsien, R.W., *Nature* 357:134-139 (1992).

Mays, R.W., *et al.*, *J. Cell Biol.* 130:1105-1115 (1995).

Pevsner, J., *et al.*, *Neuron* 13:353-361 (1994a).

Pevsner, J., *et al.*, *Proc. Natl. Acad. Sci. USA* 91:1445-1449 (1994b).

Scheller, R.H., *Neuron* 14:893-897 (1995).

Stone, K.L., and K.R. Williams, "Enzymatic Digestion of Proteins and HPLC Peptide Isolation" in A PRACTICAL GUIDE TO PROTEIN AND PEPTIDE PURIFICATION FOR MICROSEQUENCING, 2ND ED., Matsudaira, P., Ed., Academic Press, New York (1993).

TerBush, D.R., and Novick, P., *J. Cell Biol.* 130:299-312 (1995).

TerBush, D.R., *et al.*, *EMBO J.* 15:6483-6494 (1996).

Ting, A.E., *et al.*, *Proc. Natl. Acad. Sci. USA* 92:9613-9617 (1995).

Background of the Invention

Signal transmission between nerve cells typically involves the release of neurotransmitter from a presynaptic cell onto a postsynaptic cell. The neurotransmitter in the presynaptic cell is contained in synaptic vesicles positioned above the release sites at the presynaptic membrane (active zones). In response to a release signal (typically a local influx of calcium due to a depolarization of the presynaptic terminal), the vesicles undergo a series of mobilization steps culminating in the fusion of the vesicles with the presynaptic terminal membrane, and a dumping of vesicle contents into the synaptic cleft.

The neurotransmitter molecules diffuse across the synaptic cleft and bind to corresponding receptors in the postsynaptic membrane to communicate the appropriate signal (typically a depolarization or hyperpolarization of the postsynaptic membrane) to the postsynaptic cell. Much of the neurotransmitter in the synapse is subsequently re-absorbed by the presynaptic cell through specific transmitter uptake mechanisms.

A number of drugs affecting signalling in the central nervous system (CNS) and the peripheral nervous system (PNS) have been developed. Some of these, such as phenoxybenzamine, block specific post-synaptic receptors; others, such as clonidine and diethylamide, stimulate such receptors; still others (*e.g.*, desipramine, imipramine) act on reuptake mechanisms, and some act on neurotransmitter synthesis (*e.g.*, α-Methyltyrosine, p-Chlorophenylalanine) or degradation (*e.g.*, monoamine oxidase inhibitors, iproniazid, pargyline).

The present invention provides a tool for the screening and identification of drugs capable of affecting secretory processes, such as neurotransmitter release at the active zones of presynaptic membranes.

Summary of the Invention

In one aspect, the present invention includes a method of identifying a compound capable of modulating secretion of secretory vesicles. The method includes contacting an SA-17S complex with an SC complex, in the presence and absence of a test compound, measuring the effect of the test compound on the extent of binding between the SA-17S and the SC complexes, and identifying the compound as effective if its measured effect on the extent of binding is above a threshold level.

In one embodiment, the SA-17S complex binds to the 7S SC complex. In another embodiment, the SA-17S complex binds to the 20S SC complex.

The test compound may be effective to enhance (potentiate) or inhibit binding between the SA-17S and SC complexes. Compounds tested may include small molecules in a small molecule

combinatorial library, peptides (*e.g.*, peptides in a peptide combinatorial library), and the like. A compound which enhances binding between the SA-17S and SC complexes may be used to treat an affective disorder (such as depression, manic-depressive disorders and anxiety disorders) or a neurodegenerative disease (such as Parkinson's disease or Huntington's disease). A compound which inhibits binding between the SA-17S and SC complexes may be used to treat a disorder of thought, such as schizophrenia.

In another aspect, the invention includes a substantially purified SA-17S p71 polypeptide, having a molecular weight of about 71 kD and having the sequence of SEQ ID NO:54.

In another aspect, the invention includes a substantially purified SA-17S p79 polypeptide, having a molecular weight of about 79 kD and having the sequence of SEQ ID NO:56.

In another aspect, the invention includes a substantially purified SA-17S p84 polypeptide, having a molecular weight of about 84 kD and having the sequence of SEQ ID NO:58.

In another aspect, the invention includes a substantially purified SA-17S p96 polypeptide, having a molecular weight of about 96 kD and having the sequence of SEQ ID NO:60.

In another aspect, the invention includes a substantially purified SA-17S p102 polypeptide, having a molecular weight of about 102 kD and having the sequence of SEQ ID NO:62.

In another aspect, the invention includes a substantially purified SA-17S p106 polypeptide, having a molecular weight of about 106 kD and characterized by at least one sequence selected from the group consisting of SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, and SEQ ID NO:52.

In another aspect, the invention includes a substantially purified polypeptide having (i) at least 60% sequence identity with a selected one of the SA-17S polypeptides p71, p79, p84, p96, p102, and p106, and (ii) the property of the selected polypeptide to form an SC-binding SA-17S complex when combined stoichiometrically with the other polypeptide components of the SA-17S complex.

In another aspect, the invention includes a substantially purified polynucleotide having the sequence SEQ ID NO:53 encoding the SA-17S p71 polypeptide.

In another aspect, the invention includes a substantially purified polynucleotide having the sequence SEQ ID NO:55 encoding the SA-17S p79 polypeptide.

In another aspect, the invention includes a substantially purified polynucleotide having the sequence SEQ ID NO:57 encoding the SA-17S p84 polypeptide.

In another aspect, the invention includes a substantially purified polynucleotide having the sequence SEQ ID NO:59 encoding the SA-17S p96 polypeptide.

In another aspect, the invention includes a substantially purified polynucleotide having the sequence SEQ ID NO:61 encoding the SA-17S p102 polypeptide.

In another aspect, the invention includes a substantially purified polynucleotide (i) having at least 60% sequence identity with a selected one of the polynucleotides encoding p71, p79, p84, p96, and p102, and (ii) encoding a polypeptide having the property of the polypeptide encoded by the selected polynucleotide to form an SC-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

In another aspect, the invention includes substantially purified antibodies, such as polyclonal or monoclonal antibodies, which are specifically-immunoreactive with one of the proteins or polypeptides described above.

These and other objects and features of the invention will become more fully apparent when the following detailed description is read in conjunction with the accompanying drawings.

Brief Description of the Figures

Fig. 1A shows a Coomassie blue-stained protein profile of glycerol gradient fractions from rat brain supernatant separated on a linear glycerol gradient, and analyzed by SDS-PAGE followed by Western blotting, with positions of rsec8, rsec6 and nsec1 on the gel indicated on the right as 8, 6, and 1 respectively. Fig. 1B shows immunodetection of rsec6, rsec8 and nsec1 in gradient fractions using immunoaffinity-purified antibodies, with size markers indicated by arrows. Fig. 1C shows co-immunoprecipitation of rsec6 and rsec8.

Figs. 2A, 2B and 2C show the purification of rat brain SA-17S complex. Fig. 2A shows Coomassie blue-stained SDS polyacrylamide gel analysis of pooled column fractions. Fig. 2B shows a Western blot analysis of the column fractions shown in Fig. 2A. Fig. 2C shows a Coomassie blue-stained SDS polyacrylamide gel analysis of purified SA-17S complex.

Figs. 3A, 3B, 3C and 3D show mass spectrometric analyzes of SA-17S complex peptides p102, p96, p71 and p84, respectively, with the mass of each peptide predicted by mass spectrometry shown above the peptide peak. The amino acid sequence of each peptide determined by peptide sequencing and its mass (protonated form of peptide) calculated from the determined peptide sequence is shown beside corresponding peptide peak.

Figs. 4A-4H show peptide sequences from the following SA-17S complex peptides, respectively: rsec8, p106, p102, p96, rsec6, p84, p79, and p71.

Fig. 5A shows a Western blot analysis of brain regional expression of the SA-17S complex. Fig. 5B shows the presence of the SA-17S complex in cultured cell lines, indicated.

Fig. 6A shows a Western blot analysis of subcellular fractionation of the SA-17S complex. Fig. 6B shows association of the SA-17S complex with brain membranes as analyzed by Western blot Fig. 6C shows the nature of rsec8 association with brain membranes. Fig. 6D shows immunoprecipitation of synaptic vesicles from rat brain supernatant with anti-SV2 antibody or control mouse immunoglobulin coupled to Dynabeads M-500.

Figs. 7A-D shows cultures of primary hippocampal neurons fixed and immunostained with antibodies against rsec8 (Figs. 7A and 7B) and synaptotagmin (Fig 7 C). Fig. 7D shows a larger magnification of rsec8 staining overlaid with that of synaptotagmin at two synaptic terminals indicated by arrows. Bars = 7μm.

Fig. 8A is a Western blot analysis using seven monoclonal antibodies generated against rsec8 showing that syntaxin associates with the SA-17S complex. Fig. 8B shows a co-immunoprecipitation of syntaxin with rsec8.

Brief Description of the Sequences

SEQ ID NO:1 is the nucleotide sequence of rsec6.

SEQ ID NO:2 is the amino acid sequence of rsec6.

SEQ ID NO:3 is the nucleotide sequence of rsec8.

SEQ ID NO:4 is the amino acid sequence of rsec8.

SEQ ID NO:5 is the amino acid sequence of peptide fragment rsec6.1.

SEQ ID NO:6 is the amino acid sequence of peptide fragment rsec6.2.

SEQ ID NO:7 is the amino acid sequence of peptide fragment rsec6.3.

SEQ ID NO:8 is the amino acid sequence of peptide fragment rsec8.1.

SEQ ID NO:9 is the amino acid sequence of peptide fragment rsec8.2.

SEQ ID NO:10 is the amino acid sequence of peptide fragment rsec8.3.

SEQ ID NO:11 is the amino acid sequence of peptide fragment p71.1.

SEQ ID NO:12 is the amino acid sequence of peptide fragment p71.2.

SEQ ID NO:13 is the amino acid sequence of peptide fragment p71.3.

SEQ ID NO:14 is the amino acid sequence of peptide fragment p79.1.

SEQ ID NO:15 is the amino acid sequence of peptide fragment p79.2.

SEQ ID NO:16 is the amino acid sequence of peptide fragment p79.3.

SEQ ID NO:17 is the amino acid sequence of peptide fragment p79.4.

SEQ ID NO:18 is the amino acid sequence of peptide fragment p79.5.

SEQ ID NO:19 is the amino acid sequence of peptide fragment p79.6.

SEQ ID NO:20 is the amino acid sequence of peptide fragment p79.7.
SEQ ID NO:21 is the amino acid sequence of peptide fragment p79.8.
SEQ ID NO:22 is the amino acid sequence of peptide fragment p79.9.
SEQ ID NO:23 is the amino acid sequence of peptide fragment p79.10.
SEQ ID NO:24 is the amino acid sequence of peptide fragment p84.1.
SEQ ID NO:25 is the amino acid sequence of peptide fragment p84.2.
SEQ ID NO:26 is the amino acid sequence of peptide fragment p84.3.
SEQ ID NO:27 is the amino acid sequence of peptide fragment p84.4.
SEQ ID NO:28 is the amino acid sequence of peptide fragment p84.5.
SEQ ID NO:29 is the amino acid sequence of peptide fragment p84.6.
SEQ ID NO:30 is the amino acid sequence of peptide fragment p84.7.
SEQ ID NO:31 is the amino acid sequence of peptide fragment p84.8.
SEQ ID NO:32 is the amino acid sequence of peptide fragment p84.9.
SEQ ID NO:33 is the amino acid sequence of peptide fragment p96.1.
SEQ ID NO:34 is the amino acid sequence of peptide fragment p96.2.
SEQ ID NO:35 is the amino acid sequence of peptide fragment p96.3.
SEQ ID NO:36 is the amino acid sequence of peptide fragment p96.4.
SEQ ID NO:37 is the amino acid sequence of peptide fragment p96.5.
SEQ ID NO:38 is the amino acid sequence of peptide fragment p102.1.
SEQ ID NO:39 is the amino acid sequence of peptide fragment p102.2.
SEQ ID NO:40 is the amino acid sequence of peptide fragment p102.3.
SEQ ID NO:41 is the amino acid sequence of peptide fragment p102.4.
SEQ ID NO:42 is the amino acid sequence of peptide fragment p102.5.
SEQ ID NO:43 is the amino acid sequence of peptide fragment p102.6.
SEQ ID NO:44 is the amino acid sequence of peptide fragment p102.7.
SEQ ID NO:45 is the amino acid sequence of peptide fragment p106.1.
SEQ ID NO:46 is the amino acid sequence of peptide fragment p106.2.
SEQ ID NO:47 is the amino acid sequence of peptide fragment p106.3.
SEQ ID NO:48 is the amino acid sequence of peptide fragment p106.4.
SEQ ID NO:49 is the amino acid sequence of peptide fragment p106.5.
SEQ ID NO:50 is the amino acid sequence of peptide fragment p106.6.
SEQ ID NO:51 is the amino acid sequence of peptide fragment p106.7.
SEQ ID NO:52 is the amino acid sequence of peptide fragment p106.8.

SEQ ID NO:53 is the nucleotide sequence encoding p71 (rsec10).

SEQ ID NO:54 is the amino acid sequence of p71 (rsec10).

SEQ ID NO:55 is the nucleotide sequence encoding p79 (rexo70).

SEQ ID NO:56 is the amino acid sequence of p79 (rexo70).

SEQ ID NO:57 is the nucleotide sequence encoding p84 (rexo84).

SEQ ID NO:58 is the amino acid sequence of p84 (rexo84).

SEQ ID NO:59 is the nucleotide sequence encoding p96 (rsec15).

SEQ ID NO:60 is the amino acid sequence of p96 (rsec15).

SEQ ID NO:61 is the nucleotide sequence encoding p102 (rsec5).

SEQ ID NO:62 is the amino acid sequence of p102 (rsec5).

Detailed Description of the Invention

I. Definitions

"Substantially purified" refers to the at least partial purification of a selected polynucleotide, polypeptide, or related compound away from unrelated or contaminating components (*e.g.*, serum cells, other proteins).

When a first polynucleotide fragment or polypeptide fragment is said to "correspond to" a second polynucleotide fragment or polypeptide fragment, respectively, it means that the fragments or regions are essentially co-extensive with one another when the sequences representing the fragments are aligned using a sequence alignment program, such as "MACVECTOR" (IBI, New Haven, CT). "Corresponding" polynucleotide or polypeptide fragments typically contain a similar, if not identical, number of residues. It will be understood, however, that corresponding fragments may contain insertions or deletions of residues with respect to one another, as well as some differences in their sequences.

The term "significant", when used with reference to "significantly different", "significantly inhibits" or "significantly stimulates", refers to a difference in a quantifiable parameter between the two groups being compared that is statistically-significant using standard statistical tests. For example, the degree of binding in a protein binding assay may be quantified using standard methods, and the degree of binding under different conditions can be compared for statistically-significant differences.

An antibody or antibody composition (*e.g.*, polyclonal antibodies) is "specifically immunoreactive" with a selected protein when the antibody or antibody composition is not reactive with antigens typically present in normal sera, not exposed to the selected protein.

A "syntaxin-containing complex", or "SC complex", refers to a complex formed of one or more proteins, where one of the proteins is syntaxin (Bennett, *et al.*, 1993; Scheller, 1995). Exemplary SC complexes include the 7S complex (comprising VAMP, synaptotagmin, syntaxin and SNAP-25) and the 20S complex (comprising VAMP, syntaxin, SNAP-25, α-SNAP and NSF).

A polypeptide is "characterized by" a selected sequence when the polypeptide contains a sequence that is identical or substantially identical to the selected sequence.

"SNAP-25" refers to synaptosomal-associated protein of 25 kDa (Pevsner, *et al.*, 1994a; Scheller, 1995).

"α-SNAP" refers to soluble NSF attachment protein (Pevsner, *et al.*, 1994a; Scheller, 1995).

"NSF" refers to *N*-ethylmaleimide-sensitive factor (Pevsner, *et al.*, 1994a; Scheller, 1995).

"VAMP" refers to vesicle-associated membrane protein (Pevsner, *et al.*, 1994a; Scheller, 1995).

II. Analysis, Isolation and Purification of the SA-17S Complex

Experiments performed in support of the present invention and described in detail below have resulted in the identification of proteins that are involved in both regulated and constitutive exocytosis. Specifically, it has been discovered that in mammalian brain, the proteins rsec6 and rsec8, together with p71, p79, p84, p96, p102 and p106 proteins, are present in a high molecular weight complex, termed secretion-associated 17S (SA-17S) complex.

Analysis of the rat brain SA-17S complex revealed that it contains both rsec6 and rsec8. As described in Example 1, soluble brain proteins were fractionated on a linear glycerol gradient and the gradient fractions were analyzed by both sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and Western blotting. A Coomassie blue-stained protein profile of the fractions is shown in Figure 1A. The migration of rsec6 and rsec8 in the gradient was monitored by Western blot analysis using affinity-purified anti-rsec6 and anti-rsec8 antibodies. The results are shown in Figure 1B. Both rsec6 and rsec8 migrated at the 17S position. To determine if the co-fractionating rsec6 and rsec8 were in the same complex, rsec6 and rsec8 were immunoprecipitated from polyethylene glycol-fractionated rat brain supernatant with affinity-purified antibodies against rsec8 or with control rabbit immunoglobulin. The immunoprecipitated sample was analyzed for the presence of rsec6, rsec8 and nsec1 by Western blotting. The results, shown in Figure 1C, demonstrate that rsec6, but not nsec1, co-immunoprecipitated with rsec8 from soluble brain proteins using affinity-purified rabbit polyclonal anti-rsec8 antibodies. Taken together, these

data demonstrate that both rsec6 and rsec8 are components of the same high molecular weight complex.

Experiments detailed in Example 2 describe the purification of the SA-17S complex, and show that the complex is formed of 8 separate proteins or polypeptides. The SA-17S complex was purified from frozen rat brain by four sequential column chromatographic steps. The enrichment of the SA-17S complex following each chromatographic step was monitored by Western blot analysis using mouse polyclonal antibodies against rsec6 and rsec8, as shown in Figure 2B. After completing the steps detailed in Example 2, eight polypeptides of molecular weights 71, 79, 84, 86, 96, 102, 106, and 110 kDa were apparent in a Coomassie blue stained SDS-PAGE gel. These proteins were termed SA-17S p71, SA-17S p79, SA-17S p84, SA-17S p86, SA-17S p96, SA-17S p102, SA-17S p106, and SA-17S p110, respectively. Subsequent peptide sequence analyses, described below, determined that SA-17S p110 was rsec8 and SA-17S p86 was rsec6. SDS-PAGE analysis of pooled peak rsec6 and rsec8 immunoreactivity fractions indicated that these eight proteins constituted at least 95% of the total proteins in this fraction (Figure 2A, lane TMAE2; Figure 2C).

Fractionation of the purified complex on a glycerol gradient demonstrated that all eight components co-migrate at the 17S position. In addition, all eight proteins co-immunoprecipitated with rsec8 monoclonal antibodies. Further, all eight proteins were approximately equally stained by Coomassie blue, suggesting a stoichiometry of one copy of each protein within the complex (Figure 2C). This 1:1 stoichiometry is further supported by the apparent molecular weight of the native complex (~600-700 kD).

The SA-17S is also unusually stable, with monomeric forms of the proteins forming the complex never observed under non-denaturing conditions. Unlike the 20S particle composed of syntaxin, VAMP, SNAP-25, α-SNAP and NSF, the SA-17S complex does not dissociate in response to ATP hydrolysis. In fact, this complex does not dissociate in the presence of ATP, GTP, ATPγS, GTPγS, EGTA and/or Ca^{2+}. The mammalian SA-17S complex is found in soluble and membrane-bound states.

III. Polypeptides Contained in the SA-17S Complex

To further characterize individual components of the mammalian SA-17S complex, the purified complex was fractionated on an SDS polyacrylamide gel and each protein band was cut out and individually subjected to in-gel proteolysis as described in Example 3, to generate peptides which could be further characterized by high performance liquid chromatography (HPLC), mass spectrometry for peptide purity and mass, and peptide sequencing.

Figures 3A, 3B, 3C and 3D show the mass spectrometric analyzes of HPLC peptide peaks from four proteins, SA-17S p102, SA-17S p96, SA-17S p84 and SA-17S p71, respectively, with the mass of each peptide predicted by mass spectrometry is shown above the peptide peak. The amino acid sequence of each peptide determined by peptide sequencing and its mass (protonated form of peptide) calculated from the determined peptide sequence is shown beside corresponding peptide peak, along with its SEQ ID NO. In Panels A to C the calculated and observed masses matched with less than 0.1% difference. Peptide sequences obtained from the eight members of the SA-17S complex are shown in Figures 4A-H, as well as Tables 1-8, below.

These sequences, as well as the molecular weights of the polypeptides, are effective to uniquely characterize the 8 proteins which form the SA-17S complex. In this respect, the invention includes the following substantially purified polypeptides: (i) SA-17S p71 polypeptide, having a molecular weight of about 71 kD and characterized by at least one sequence selected from the group consisting of SEQ ID NO:11, SEQ ID NO:12 and SEQ ID NO:13; (ii) SA-17S p79 polypeptide, having a molecular weight of about 79 kD and characterized by at least one sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22 and SEQ ID NO:23; (iii) SA-17S p84 polypeptide, having a molecular weight of about 84 kD and characterized by at least one sequence selected from the group consisting of SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, and SEQ ID NO:32; (iv) SA-17S p96 polypeptide, having a molecular weight of about 96 kD and characterized by at least one sequence selected from the group consisting of SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36 and SEQ ID NO:37; (v) SA-17S p102 polypeptide, having a molecular weight of about 102 kD and characterized by at least one sequence selected from the group consisting of SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, and SEQ ID NO:44; and (v) SA-17S p106 polypeptide, having a molecular weight of about 106 kD and characterized by at least one sequence selected from the group consisting of SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, and SEQ ID NO:52.

These peptides are useful for the formation of a complete SA-17S complex, which can be employed, *e.g.*, in screens such as the screen described below. The peptides may also be used to identify the site of interaction between the SA-17S and SC complexes, enabling the design of a simpler screen for compounds which modulate such an interaction.

A. Isolation of Full-length Clones Encoding SA-17S Polypeptides

The peptide sequences provided in Tables 1-8, below, were used to isolate DNA or cDNA clones encoding the complete proteins, according to standard techniques. From these studies, polynucleotide sequences which encode full-length SA-17S polypeptides p71, p79, p84, p96, and p102. Based on amino acid sequence similarities, six of the eight components of the mammalian SA-17S complex have counterparts in the 834 kDa yeast Sec6/8/15 complex (TerBush and Novick, 1995; TerBush, *et al.*, 1996).

The SA-17S p71 cDNA (SEQ ID NO:53) has an open reading frame (ORF) which encodes a 708 amino acid polypeptide (SEQ ID NO:54) with a calculated molecular weight of 82 kdal. The p71 polypeptide is homologous to yeast sec10 and is thus denoted rsec10. The amino acid sequence contains potential coiled-coil domains at the N-terminus and near the C-terminus of the protein. In addition, rsec10 is homologous with the tail domain of yeast type II myosin, and may interact with cytoskeletal proteins.

The SA-17S p79 cDNA (SEQ ID NO:55) has an ORF which encodes a 653 amino acid protein (SEQ ID NO:56) with a calculated molecular weight of 75 kDa. The p79 polypeptide sequence shows 23% identity and 33% similarity to yeast exo70 and is thus denoted rexo70. Using the Coils 2.1 program, a region of 30 amino acids (residues 5-34) at the amino terminus of the protein is predicted to have a high probability (between 0.88 and 1.0) of forming a coiled-coil domain, a structure which is known to be involved in protein-protein interactions.

The SA-17S p96 cDNA (SEQ ID NO:59) has an ORF which encodes an 822 amino acid protein (SEQ ID NO:60) with a calculated molecular weight of 95 kDa. The p96 protein sequence shows 24% identity and 36% similarity to yeast sec15 and is designated rsec15. A region of 22 amino acids (residues 85-106) at the amino terminus of the protein has a probability of greater than 0.59 to form a coiled-coil domain.

The SA-17S p102 cDNA (SEQ ID NO:61) has an ORF which encodes a 924 amino acid protein (SEQ ID NO:62) with a calculated molecular weight of 104 kDa. The p102 protein sequence shows 21% identity and 32% similarity to yeast sec5, and is denoted rsec5. A region of 21 amino acids (residues 240-260) at the amino terminus of the protein has a high probability (greater than 0.94) to form a coiled-coil domain.

The cDNA sequence of the SA-17S p84 subunit (SEQ ID NO:57) was identified based on overlapping rat cDNA clones which encode the peptide sequences derived from the p84 subunit (SEQ ID NO:24-32). The predicted protein (SEQ ID NO:58) is designated rexo84 since it corresponds to the 84 kDa protein in the complex. Like other proteins of the SA-17S complex,

rexo84 contains regions predicted to form coiled-coils. The rexo84 sequence is not significantly similar to any of the known components of the 834 kDa yeast Sec6/8/15 complex.

All the above-identified members of the mammalian SA-17S complex, as well as rsec6 and rsec8, contain regions predicted to form coiled-coil domains, suggesting that subunits in this complex interact with each other at least in part via these domains. Predicted coiled-coil domains are prominent in other membrane trafficking proteins including the SNAREs, suggesting these interactions may be involved in inter-complex interactions as well.

B. Recombinant Production of the SA-17S Proteins

Polynucleotide sequences encoding proteins of the SA-17S complex may be cloned into an expression plasmid, such as a p-GEX plasmid (Pharmacia), to produce corresponding polypeptides. Recombinant pGEX plasmids can be transformed into appropriate strains of *E. coli* and fusion protein production can be induced by the addition of IPTG (isopropyl-thio galactopyranoside). Solubilized recombinant fusion protein can then be purified from cell lysates of the induced cultures using glutathione agarose affinity chromatography according to standard methods (Ausubel, *et al.*, 1992).

Affinity chromatography may also be employed for isolating β-galactosidase fusion proteins (such as those produced by lambda gt11 clones). The fused protein is isolated by passing cell lysis material over a solid support having surface-bound anti-β-galactosidase antibody.

Isolated recombinant polypeptides produced as described above may be purified by standard protein purification procedures. These procedures may include differential precipitation, molecular sieve chromatography, ion-exchange chromatography, isoelectric focusing, gel electrophoresis and affinity chromatography.

In addition to recombinant methods, SA-17S complex proteins or polypeptides can be isolated from selected cells by affinity-based methods, such as by using appropriate antibodies (described below). Further, SA-17S complex peptides may be chemically synthesized using methods known to those skilled in the art.

C. Antibodies Directed Against SA-17S Polypeptides

SA-17S polypeptides of the present invention, such as polypeptides identified by sequences SEQ ID NO:5-52, as well as full-length polypeptides corresponding to one of the eight protein components of SA-17S, such as polypeptides identified by sequences SEQ ID NO:2, 4, 54, 56, 58, 60, and 62, and fragments thereof, may be used in the generation of antibodies, *e.g.*, as described in

the Materials and Methods below. The polypeptides may be used in unmodified form, or they may be coupled to appropriate carrier molecules, such as bovine serum albumin (BSA) or Keyhole Limpet Hemocyanin (KLH) (available from, for example, Pierce, Rockford, IL).

To prepare antibodies, a host animal, such as a mouse or rabbit, is typically immunized with the purified polypeptide, or polypeptide coupled to carrier or fusion protein (*e.g.*, a His-tagged fusion protein or a glutathione-S-transferase fusion). The host serum or plasma is collected following an appropriate time interval, and the serum is tested for antibodies specific against the polypeptide.

The gamma globulin fraction or the IgG antibodies of immunized animals can be obtained, for example, by use of saturated ammonium sulfate precipitation or DEAE Sephadex chromatography, affinity chromatography, or other techniques known to those skilled in the art for producing polyclonal antibodies.

Alternatively, purified antigenic polypeptide or fused antigen protein may be used for producing monoclonal antibodies. In this case, the spleen or lymphocytes from an immunized animal are removed and immortalized or used to prepare hybridomas by methods known to those skilled in the art (*e.g.*, Harlow, *et al.*, 1988). For example, hybridomas may be prepared by fusion of NS-1 mouse myeloma cells with spleen cells from BALB/c mice immunized with His-tagged fusion protein (Lane, *et al.*, 1986). Antibodies secreted by the immortalized cells are screened (*e.g.*, using enzyme linked immunosorbent assay (ELISA) or a Western blot) to determine the clones that secrete antibodies of the desired specificity (*e.g.*, Ausubel, *et al.*, 1992).

If desired, the antibodies may be affinity-purified prior to use, using methods known in the art (*e.g.*, Harlow, *et al.*, 1988). Antibodies or FAb fragments thereof generated as described above may be used in a variety of ways. In particular, they can be used to detect or quantitate the level of SA-17S polypeptides in any of the methods of the present invention where such detection is contemplated, *e.g.*, in methods employing Western-based detection approaches. Further, the antibodies can be used in screens of expression libraries, as described above. The antibodies may also be used to co-immunoprecipitate proteins which interact with the SA-17S complex, as described in the Materials and Methods and Example 7.

IV. Expression Pattern of the SA-17S Complex

Expression patterns of the SA-17S complex are described below in Examples 4-6. Peripheral rsec8 staining in synaptic terminals suggests that the SA-17S complex is associated with the synaptic plasma membrane. The presence of the SA-17S complex in hippocampal synapses,

together with its association with the synaptosomal protein syntaxin, indicate that the SA-17S complex plays a critical role in the synaptic vesicle trafficking pathway of yeast and mammals.

V. Role of the SA-17S Complex in Secretion

The SA-17S complex is required for normal secretion and synaptic release, and therefor, compounds which inhibit the association of the SA-17S complex with syntaxin or a syntaxin-containing complex will inhibit the release of the secretory vesicles.

The results of the experiments described herein, including (i) the demonstration of an *in vivo* interaction between rsec8 and syntaxin as revealed by the immunoprecipitation of syntaxin with anti-rsec8 antibodies, and (ii) selective staining of neurons with anti-rsec8 antibodies in the area near the plasma membrane of the nerve terminals (the site of exocytosis), are in agreement with studies of yeast secretory mutants. The yeast studies have revealed genetic interactions between Sec8/Sec15 and the yeast homologs of syntaxin and SNAP25, SSO1 and Sec9. Specifically, overexpression of SSO1 can suppress mutations in the SEC15 gene (Aalto, *et al.*, 1993), while over-expression of Sec9 can suppress mutations in both the SEC8 and SEC15 genes (Brennwald and Novick, 1993). Additionally, staining of the Sec6/8/15 complex in yeast appears enhanced at the site of vesicle docking and fusion in the tip of the bud.

The data presented here are also consistent with a role for the SA-17S complex in a Rab mediated event at the plasma membrane, possibly intervening between the Rab and the 7S complex (Bowser, *et al.*, 1992).

Expression of the SA-17S complex is not as high in neurons and endocrine cells as some of the isoforms of vesicle trafficking proteins involved in the synaptic vesicle docking and fusion pathway. Northern and Western blot analyses as well as fluorescence microscopy studies detect its expression in all tissues and cultured cell lines examined. This ubiquitous distribution of the SA-17S complex suggests that it is important in both constitutive and regulated membrane trafficking and that its function is fundamental to the exocytotic process.

Although the SA-17S complex is described herein as pertaining primarily to neurotransmitter release, it is contemplated that the SA-17S complex is involved in secretory release in a number of other cell types, including mast cells.

VI. Screens for Inhibitors of Synaptic Protein Interactions

The present invention includes methods of screening for compounds effective to modulate vesicular release involved in synaptic transmission and other secretory processes. The methods are

used to identify a compound capable of affecting binding of a secretion associated 17S (SA-17S) complex to a syntaxin-containing (SC) complex. An SA-17S complex is contacted with an SC complex, in the presence and absence of a test compound. The effect of the test compound on the extent of binding between the SA-17S and the SC complexes is measured, and a compound is identified as effective if its effect on the extent of binding is above a threshold level (*e.g.*, a several-fold difference in binding level between control and experimental samples).

The test compound may be effective to enhance (potentiate) or inhibit binding between the SA-17S and SC complexes. Compounds tested may include small molecules in a small molecule combinatorial library, peptides in a peptide combinatorial library, and the like.

Compounds which affect the binding of the SA-17S and SC complexes to one another, when applied to target cells, are expected to modulate vesicular release by those cells. The modulation may be an inhibition of release or stimulation of release, either when the compound is applied alone, or when the compound is applied in conjunction with another compound having an effect on vesicular release.

In one embodiment, the assay is conducted using a co-immunoprecipitation method such as is described in the Materials and Methods and Example 7. Anti-rsec8 monoclonal antibodies (such as antibodies 2E9 and/or 17A10) or mouse immunoglobulin are coupled to protein G beads at a final concentration of 2 mg/ml using the cross-linker dimethylpimelimidate (Pevsner, *et al.*, 1994a). Rat brain membranes prepared as described herein are resuspended in 20 mM Tris, pH 8.0, 150 mM NaCl and solubilized with either 1% CHAPS or Triton X-100 at a final protein concentration of 2 mg/ml.

The solubilized sample is incubated at 4°C for 30 min before centrifuging at 20,000 xg for 20 min. Following centrifugation, the solubilized brain membranes are pre-cleared by incubation with protein G beads (1 ml solubilized membranes per 200 μl protein G beads) for 30 min at 4°C. The pre-cleared supernatant is then incubated with (i) a selected concentration of the test compound and (ii) 20 μl protein G beads with either immobilized anti-rsec8 monoclonal antibodies 2E9/17A10 or immobilized control mouse Ig for 4 hrs at 4°C. The beads are then washed three times with 300 μl 20 mM Tris, pH 8.0, 150 mM NaCl containing either 0.7% CHAPS or Triton X-100. Proteins bound to the beads are analyzed by Western blotting for the presence of syntaxin as described in the Materials and Methods and Examples below.

If the test compound is effective to inhibit binding of an SC complex to the immobilized SA-17S complex, the amount of syntaxin detected in the Western blot will be diminished. Conversely, if the test compound is effective to enhance the binding of an SC complex to the immobilized SA-

17S complex, the amount of syntaxin detected in the Western blot will be increased. The assay is typically conducted with both negative controls (*e.g.*, beads coated with control mouse Ig) and positive controls (no test compound in assays with anti-rsec8 antibody).

It will be appreciated that the co-immunoprecipitation assay may be practiced using other antibodies which recognize and can immunoprecipitate the SA-17S complex, such as anti-rsec6 antibodies or antibodies directed against one or more of the other proteins in the complex.

A. Measuring the Effect of a Test Compound on the Extent of Binding

The type of measurement used to quantify the effect of a test compound on the extent of binding between the SA-17S complex and a SC complex depends on the type of screening assay and detection system used, and can be readily determined by one of skill in the art.

For example, in a co-immunoprecipitation screen employing a Western blot detection, such as described above, the extent of binding may be measured using densitometry of the Western blot image. The densitometry values are typically normalized, and a threshold level is set based on the amount of variation in the signal between a series of "control" samples (samples not containing test compounds). The smaller the variation, the smaller the effect of a test compound that can be reliably detected. The threshold is typically set at a several-fold difference, such as a 3-5 fold increase or decrease in binding affinity.

The precise threshold level used in a particular application of the invention is determined in view of the specific requirements of that particular application. For example, if it is desired to isolate only compounds with a very high activity, the threshold is set to a relatively high value, such as a 10 to 100-fold difference in binding affinity. If, on the other hand, it is desired to isolate compounds having a subtle effect on the binding, a lower threshold level may employed.

It is also appreciated that, as with any other compound screening assay, the effect of a particular compound on the binding of a SA-17S complex to an SC complex depends on the concentration of the compound. At relatively high compound concentrations the effect may be large, and be manifested as, *e.g.*, a 50-fold difference in binding between control and experimental samples, whereas at lower compound concentrations, the effect may be smaller.

B. Effects of Identified Compounds on Vesicular Release

Compounds identified by a screen such as one described above as affecting the binding of an SA-17S complex to an SC complex may be further evaluated for their ability to modulate vesicular release *in vitro* and *in vivo*.

For example, the compounds may be tested using the PC12 cell DβH vesicular release assay (Bennett, *et al.*, 1993), which detects a membrane-associated form of the enzyme dopamine β-hydroxylase (DβH) on the luminal side of catecholamine-containing granules. When the cells are depolarized in the presence of calcium, granule fusion with the plasma membrane results in the exposure of DβH on the cell surface, where it can be quantitatively detected by immunofluorescence microscopy (Elferink, *et al.*, 1993). By treating a sample of cells with a compound identified as affecting the binding of an SA-17S complex to an SC complex, depolarizing the cells (*e.g.*, with a pulse of KCl) in the presence of calcium, and comparing the response to that obtained with an untreated sample of cells, the effects of the compound on vesicle release in PC12 cells may be assessed. Similar assays may be employed using freshly-isolated cells (*e.g.*, in brain slices), or suitable animal models.

VII. Compounds Suitable for Screening

A variety of different compounds may be screened using methods of the present invention. They include peptides, macromolecules, small molecules, chemical and/or biological mixtures, and fungal, bacterial, or algal extracts. Such compounds, or molecules, may be either biological, synthetic organic, or even inorganic compounds, and may be obtained from a number of sources, including pharmaceutical companies and specialty suppliers of libraries (*e.g.*, combinatorial libraries) of compounds.

A set of potentially-effective test peptides can be generated from overlapping peptides spanning the entire sequence of each of the proteins involved in the SA-17S complex/SC complex interaction. Such a set is likely to contain peptides which may be effective to disrupt the interactions of the SA-17S complex with the SC complex.

In cases where an identified active compound is a peptide, the peptide may be utilized to aid in the discovery of orally-active small molecule mimetics.

VIII. Applications

Inhibitory compounds isolated using methods of the present invention may be employed to inhibit vesicle-mediated secretion of molecules from cells. Similarly, compounds which enhance or potentiate the binding of SA-17S complex to syntaxin or an SC complex may be used to upregulate vesicle-mediated secretion. The ability to modulate secretion processes has utility in a variety of areas, some of which are identified below.

A. CNS Disease Applications

A number of disorders and/or conditions of the central nervous system (CNS) may be alleviated by selectively enhancing or inhibiting vesicular release in specific areas of the brain. They include affective disorders (*e.g.*, depression), disorders of thought (*e.g.*, schizophrenia) and degenerative disorders (*e.g.*, Parkinson's disease), as well as applications such as anesthesia. A variety of drugs are currently used to treat such disorders and/or conditions. Compounds identified by methods of the present invention may be used either alone, or in combination with currently used therapies to alleviate symptoms associated with the disorders.

Drugs used to treat affective disorders, which include depression, manic-depressive disorders and anxiety disorders, typically fall into three classes: (i) monoamine oxidase (MAO) inhibitors, such as phenelzine, (ii) tricyclic compounds, such as imipramine, and (iii) serotonin uptake blockers, such as fluoxetine and trazodone. All of these drugs work, at least in part, by increasing the concentration of either serotonin or biogenic amine neurotransmitters in CNS synapses of treated individuals. According to methods of the present invention, compounds which enhance or stimulate the release of serotonin or biogenic amines at selected brain synapses may be similarly effective at treating affective disorders. Such compounds may be identified by screening for compounds which enhance the binding of SA-17S or its components with an SC complex.

Disorders of thought, such as schizophrenia, have been treated with a variety of antipsychotic drugs (including phenothiazines, such as chlorpromazine, butyrphenones, such as haloperidol, xithioxanthenes, and newer drugs, such as clozapine) now known to act as blockers of dopamine receptors. According to the teachings presented herein, compounds identified as inhibitors of release of dopamine-containing vesicles, particularly vesicles released from cells having their cell bodies in the arcuate nucleus of the hypothalamus, the substantia nigra, or the ventral tegmental area, may be employed to relieve symptoms of schizophrenia. Such compounds may be identified using a screening assay such as described above, for compounds effective to inhibit the binding of SA-17S complex or its components with an SC complex.

Neurodegenerative diseases, such as Parkinson's disease and Huntington's disease, may also benefit from compounds identified according to the methods of the present invention. Parkinson's disease arises due to degeneration of the nigrostriatal pathway, raphaei nuclei, locus ceruleus, and motor nucleus of vagus, which result in a reduction of dopamine, serotonin and norepinephrine levels. The symptoms of Parkinson's may be alleviated by administering compounds identified according to the teachings presented herein as stimulating release of vesicles containing the above neurotransmitters.

B. Other Applications

In addition to applications in the CNS, compounds identified employing methods of the present invention may be used to therapeutically intervene in a variety of other systems. They include the endocrine system for treatment of hormonal imbalances, the immune system for intervention in antigen processing, secreted immunomodulators, and viral processing, as well as anti-tumor applications, such as regulation of membrane trafficking during rapid cell division.

The following examples illustrate but in no way are intended to limit the present invention.

Materials and Methods

Unless otherwise indicated, [^{125}I]goat anti-rabbit secondary antisera and the Enhanced Chemo-Luminescence (ECL) system were obtained from Amersham Corp. (Arlington, Heights, IL). Nitrocellulose paper was obtained from Schleicher and Schuell (Keene, NH). Materials for SDS-polyacrylamide gel electrophoresis (SDS-PAGE) were obtained from Bio-Rad Laboratories (Hercules, CA). Lys C and Glu C were obtained from Waco. Other chemicals were purchased from Sigma (St. Louis, MO) or United States Biochemical (Cleveland, OH).

Anti-rsec8 monoclonal antibodies (mAbs) may be generated as described herein, or may be purchased from commercial sources (*e.g.*, Transduction Laboratories, Lexington, KY).

All protein and protein complex purification procedures were carried out at 4°C unless otherwise noted.

A. Glycerol Gradient Analysis

Rat brain supernatant was fractionated on a linear glycerol gradient (Ting, *et al.*, 1995) and analyzed by Western blotting. Rat brain supernatant was prepared by homogenization in 6 ml of 40 mM Hepes (pH 7.4), 150 mM NaCl, 10% (vol/vol) glycerol, 1 mM EDTA, 1 mM dithiothreitol containing leupeptin, aprotinin, pepstatin, and phenylmethanesulfonyl fluoride each at 1 μg/ml. The homogenate was centrifuged at 1000 $\times$g for 5 min and the supernatant was centrifuged at 100,000 $\times$g for 20 min. Eighty microliters (40 μg of protein) of the resulting supernatant was layered onto a 1.2-ml ten-step 22.5-36% (vol/vol) glycerol gradient in 40 mM Hepes (pH 7.4), 150 mM NaCl, 1 mM dithiothreitol. The gradient was centrifuged at 91,000 $\times$g for 16 hours at 4°C.

Fractions (95 μl) were collected and analyzed by SDS/PAGE and Western blotting. Migration of brain rsec8, rsec6 and n-Sec1 was monitored by Western blotting using affinity-purified antibodies.

B. Purification of Rat Brain SA-17S Complex

1. Bio-Gel HT Hydroxyapatite Chromatography. Fifty frozen rat brains (Harlan, IN) were homogenized in 400 ml of homogenization buffer (20 mM Hepes, pH 7.4, 200 mM NaCl, 1 mM dithiothreitol (DTT), 0.1 mM EDTA and 0.3 mM PMSF) by eight up-and-down strokes with a Teflon/glass homogenizer. A postnuclear supernatant was obtained by centrifuging the homogenate at 5000 rpm in a JA-10 rotor (Beckman, CA) for 15 min. Soluble brain protein supernatant was obtained by centrifuging the postnuclear supernatant at 36,000 rpm in a Ti45 rotor (Beckman, CA) for one hour.

Following the centrifugation, a final concentration of 110 mM sodium phosphate, pH 7.4 was added to the supernatant before it was applied to a 25 ml hydroxyapatite (BioRad, CA) column equilibrated with the homogenization buffer containing 110 mM sodium phosphate at a flow rate of 20 ml/hr at 18°C. The column was washed with 75 ml of 0.15 M sodium phosphate in buffer A (0.15 M NaCl, and 1 mM DTT, pH 7.4) and eluted stepwise with 5 ml aliquots of 0.2M to 0.65 M phosphate in buffer A, with 50 mM phosphate increment per step. Fractions containing rsec6 and rsec8 as determined by Western blot analyzes were pooled and dialyzed twice against 2 liters of 20 mM Tris, pH 8.0, 100 mM NaCl, 0.2 mM EDTA, and 0.5 mM DTT overnight.

2. Fractogel EMD TMAE-650 (S) Chromatography. The dialyzed hydroxyapatite eluant was diluted with an equal volume of 20 mM Tris, pH 8.0 and loaded onto a 3 ml column of Fractogel TMAE anion exchange resin (EM Separations Technology, NJ) equilibrated with 20 mM Tris, pH 8.0, 50 mM NaCl, and 1 mM DTT at a flow rate of 15 ml/hr. The column was washed with 20 mM Tris, pH 8.0, 50 mM NaCl, 1 mM DTT and eluted with a linear gradient of 0 to 350 mM NaCl in 20 mM Tris, pH 8.0 and 1 mM DTT.

3. HW-55S gel Filtration Chromatography. TMAE eluant fractions enriched in rsec6 and rsec8 were pooled and fractionated over a 180 ml HW-55S gel filtration column (TosoHaas, PA) equilibrated in 20 mM Hepes, pH 7.4, 200 mM NaCl, and 1 mM DTT at a flow rate of 5 ml/hr.

4. Second Fractogel EMD TMAE-650 (S) Chromatography. rsec6 and rsec8-enriched fractions from HW-55S gel filtration column chromatography were pooled and diluted to a final buffer concentration of 20 mM Tris, pH 8.0 and 50 mM NaCl. The diluted sample was applied to and eluted from a 0.5 ml Fractogel TMAE-650 column as described above.

Fractions containing purified SA-17S complex were pooled and used for SDS-PAGE analyzes and peptide sequencing.

C. Mass Spectrometry and Peptide Sequence Analysis

Purified SA-17S complex was fractionated on an 8% SDS polyacrylamide gel. Individual protein bands were cut out and subjected to in-gel proteolysis by Lys C, trypsin and/or Glu C essentially as described by Stone and Williams (1993). Excised gel slices were dried by Speed-Vac, and 500 μl of O.1 M NH_4HCO_3 was added to each gel slice. The slices were shaken at room temperature for at least 4 hours. The wash from each gel slice was removed and saved. An additional 500 μl of O.1 M NH_4HCO_3 was added to each gel slice, incubated overnight with shaking, and the wash removed and saved. A final 150 μl of O.1 M NH_4HCO_3 was added to each gel slice, plus 5 μl of 45 mM dithiothreitol. The gel slices were incubated at 50°C for 20 min., and cooled to room temperature. After addition of 5 μl 100 mM iodoacetamide, the slices were incubated in the dark at room temperature for 20 min. Proteolytic enzyme (Lys C, trypsin and/or Glu C) was added in a 1:25 weight-to-weight ratio of enzyme:protein (with a typical gel slice containing 8-10 μg of protein). After incubating the gel slices overnight at 37°C, 500 μl of O.1 M NH_4HCO_3 was added. The gel slices were shaken for 8 hr to extract the peptides. The supernatant was transferred to a tube, and 300 μl 2M urea in O.1 M NH_4HCO_3 was added to each gel slice. After 24 hr, the supernatant was transferred to the corresponding tube. The combined supernatants were dried in a Speed-Vac and redissolved in 210 μl H_2O. The digested peptides were fractionated by HPLC (Applied Biosystems). Selected peptide peaks were then subjected to amino acid sequencing by Edman degradation method (Applied Biosystems, CA). Following digestion, some peptides from p106, p96 and p79 were also fractionated on a 1090 HPLC (Hewlett-Packard). Selected HPLC fractions were subjected to MALDI-TOF mass analysis (Hewlett-Packard). Following mass spectrometric analysis, selected peptide fractions were subjected to amino acid sequencing (Hewlett Packard).

D. Brain Regional and Tissue Culture Cell Western Blot Analysis

For brain regional Western blot analysis, various rat brain regions were dissected from fresh brain and sonicated in 10 mM Hepes, pH 7.4, 2.5 mM KOAc, 1 mM $MgCl_2$, 0.1 mM EGTA, and 0.3 mM PMSF. The homogenates were centrifuged at 10,000 xg for 5 min and the postnuclear supernatants were collected.

For Western blot analysis of the rsec8 distribution in various cultured cells, tissue culture cells were grown to confluency in 10 cm petri dishes, scraped, and dounce homogenized in 20 mM Hepes, pH 7.4. The homogenates were centrifuged at 5000 xg for 5 min and the supernatants were collected for Western blot analysis.

Protein samples were electrophoresed on 12.5% resolving SDS-polyacrylamide (denaturing) gels, transferred to nitrocellulose paper (0.2 μM), and probed as described below. Proteins were visualized by enhanced chemiluminescence (ECL) system (Amersham Corp., Arlington, Heights, IL) and/or by autoradiography using ^{125}I-labeled goat anti-rabbit antibodies as the secondary antibody. Protein bands were quantitated by densitometry and/or phosphorimaging (Molecular Dynamics, Sunnyvale, CA).

E. Subcellular Localization of SA-17S Complex

For brain subcellular fractionation studies, postnuclear supernatant and crude synaptosomal membrane fractions were prepared as described (Bennett, *et al.*, 1992). Soluble brain proteins and brain membranes were obtained by centrifuging the postnuclear supernatant or lysed crude synaptosomal fraction at 100,000 xg for 20 min in a TLS 55 rotor (Beckman, CA) at 4°C. All protein samples were subjected to SDS-PAGE and Western blot analysis.

For brain membrane extraction studies, lysed brain membranes resuspended in 20 mM Tris, pH 8.0, 1 mM DTT and 10% sorbitol (2 mg/ml) were incubated with equal volumes of either 20 mM Tris, pH 8.0, 3 M NaCl in 20 mM Tris, pH 8.0, 8% Triton X-100 in 20 mM Tris, pH 8.0, or 8 M urea in 20 mM Tris, pH 8.0. The incubations were carried out at 4°C for 1 hr. Following the incubation, the membranes were pelleted at 50,000 xg. The resulting supernatants and membrane pellets were analyzed for their rsec8 content by Western blot.

The amount of rsec8 extracted from membranes were quantitated by phosphorimaging using ^{125}I-labeled secondary antibodies. The pixel values for 20 mM Tris extraction were 6713 for supernatant and 173171 for pellet; for 1.5 M NaCl extraction were 39189 for supernatant and 45414 for pellet; for Triton X-100 extraction were 56302 for supernatant and 37254 for pellet; and for urea extraction were 71419 for supernatant and 9999 for pellet.

For sucrose gradient flotation analysis of SA-17S complex, lysed crude synaptosomal membranes were resuspended in 55% sucrose in gradient buffer (20 mM Hepes, pH 7.4, 150 mM NaCl and 1 mM DTT) at a protein concentration of 4 mg/ml. The resuspended membranes were placed at the bottom of a linear 25-52.5% sucrose gradient. After centrifugation at 42,000 rpm for 16 hrs in a TLS 55 rotor (Beckman, CA), the gradient was fractionated and analyzed by Western

blot for rsec6, rsec8, Na/K ATPase (a plasma membrane marker) and synaptophysin (a synaptic vesicle marker).

F. Immunoprecipitation Studies

1. Immunoprecipitation of the SA-17S Complex. Immunoaffinity purified anti-rsec8 antibodies (Ting, *et al.*, 1995) or purified rabbit immunoglobulin were coupled to protein A beads at a final concentration of 0.5 mg/ml as previously described (Pevsner, *et al.*, 1994a; Pevsner, *et al.*, 1994b). Three ml of rat brain supernatant (Ting, *et al.*, 1995) was precipitated with 5% polyethylene glycol 3000 at 4°C and centrifuged at 20,000 xg for 10 min. The pellet was dissolved in 1 ml 20 mM Tris, pH 8.0 and 50 mM NaCl and pre-cleared by incubation with 200 μl protein A beads for 4 hrs at 4°C. Following incubation, 500 μl of pre-cleared brain supernatant was incubated with 30 μl of either anti-rsec8 antibody or rabbit immunoglobulin coupled to protein A beads overnight at 4°C. The beads were then washed three times with 200 μl 20 mM Tris, pH 8.0, 150 mM NaCl and 0.05% Tween 20. Proteins bound to the beads were solubilized in protein sample buffer, and subjected to Western blot analysis.

2. Immunoprecipitation of Synaptic Vesicles. Four frozen rat brains were powderized in liquid nitrogen using a Waring blender. The powderized brain was then homogenized in 20 ml of 0.3 M sucrose and 10 mM Hepes, pH 7.5 with a Teflon-glass homogenizer. The homogenate was centrifuged at 100,000 xg for 1 hr and the supernatant was incubated for 2 hrs at 4°C with 50 μl of anti-SV2 monoclonal antibody or purified mouse immunoglobulin coupled Dynabeads M-500 (Dynal, Oslo; 16 μg antibody/50 μl beads) in 0.3 M sucrose, 10 mM Hepes, pH 7.5 and 0.15% bovine serum albumin. Following incubation, the beads were washed four times with 0.3 M sucrose, 10 mM Hepes, pH 7.5 and solubilized in protein sample buffer. Protein samples were subjected to SDS-PAGE and analyzed by Western blotting.

3. Co-immunoprecipitation of syntaxin and the SA-17S complex. Anti-rsec8 monoclonal antibodies 2E9 and 17A10 or mouse immunoglobulin were coupled to protein G beads at a final concentration of 2 mg/ml using the cross-linker dimethylpimelimidate as previously described (Pevsner, *et al.*, 1994a). Rat brain membranes prepared as described above were resuspended in 20 mM Tris, pH 8.0, 150 mM NaCl and solubilized with either 1% CHAPS or Triton X-100 at a final protein concentration of 2 mg/ml. The solubilized sample was incubated at 4°C for 30 min before centrifuging at 20,000 xg for 20 min. Following centrifugation, the solubilized brain membranes

were pre-cleared by incubation with protein G beads (1 ml solubilized membranes per 200 μl protein G beads) for 30 min at 4°C. The pre-cleared supernatant was then incubated with 20 μl protein G beads with either immobilized anti-rsec8 monoclonal antibodies 2E9/17A10 or immobilized control mouse Ig for 4 hrs at 4°C. The beads were then washed three times with 300 μl 20 mM Tris, pH 8.0, 150 mM NaCl containing either 0.7% CHAPS or Triton X-100. Proteins bound to the beads were analyzed by Western blotting.

G. Monoclonal and Polyclonal Antibodies

Mouse polyclonal antibodies against rsec6 and rsec8 were generated against a His-tagged rsec6 fusion protein. The mouse serum recognizes a single band of 86 kDa in brain homogenate. This band is not present when pre-immune serum was used as the primary antibody.

Mouse polyclonal antibodies against rsec8 were generated against a His-tagged rsec8 fusion protein. The immunized but not pre-immune mouse serum recognizes one single band at 110 kDa in brain homogenate.

Monoclonal antibodies against rsec8, including antibodies 2E9 and 17A10, were obtained from the corresponding hybridoma cell lines generated by fusion of NS-1 mouse myeloma cells with spleen cells from BALB/c mice immunized with His-tagged rsec8 fusion protein (Lane, *et al.*, 1986).

Rabbit polyclonal antibodies against rsec8 were generated and affinity-purified as described (Ting, *et al.*, 1995).

Polyclonal antibodies against nsec1 were affinity purified as described (Pevsner, *et al.*, 1994b).

Rabbit polyclonal antibodies against Na/K ATPase (Mays, *et al.*, 1995) was obtained from Dr. W. James Nelson. Monoclonal antibody against SV2 (Buckley and Kelly, 1985) was obtained from Dr. Kathy M. Buckley, and monoclonal antibody against synaptophysin was purchased from Boehringer Mannheim (Indianapolis, IN).

H. Hippocampal Cell Culture and Immunocytochemistry

Primary hippocampal CA3/CA1 cultures were obtained and maintained as described by Malgaroli and Tsien, 1992. Immunocytochemistry was carried out as previously described (Ting, *et al.*, 1995) using affinity-purified anti-rsec8 mouse polyclonal antibodies at 0.01 μg/ml and affinity-purified rabbit anti-synaptotagmin rabbit polyclonal antibodies at 1:1000 dilution as primary antibodies. The labeling was visualized using fluorescein-labeled donkey anti-mouse and

Cy3-labeled donkey anti-rabbit antibodies. In control experiments, identical staining procedures were used except that the cells were labeled using pre-immune sera or purified immunoglobulin of equal protein concentration as the primary antibody instead.

EXAMPLE 1

rsec6 and rsec8 are Components of the Secretion-Associated 17S (SA-17S) Complex in Brain

To determine whether rsec6 and rsec8 function together in a protein complex, soluble brain proteins were fractionated on a linear glycerol gradient and the gradient fractions were analyzed by both sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and Western blotting. A Coomassie blue-stained protein profile of the fractions is shown in Figure 1A. The positions of rsec8, rsec6 and nsec1 on the gel are indicated on the right of the figure as 8, 6, and 1 respectively. Most of the proteins fractionated between the 4.3S and 11.2S regions of the gradient.

The migration of rsec6 and rsec8 in the gradient was monitored by Western blot analysis using affinity-purified anti-rsec6 and anti-rsec8 antibodies. The results are shown in Figure 1B. Fraction 1 corresponds to the top of the gradient. Size markers (indicated by the arrows) from left to right are bovine serum albumin (4.3S), β-amylase (11.2S) and thyroglobulin (19.2S). Both rsec6 and rsec8 migrated at the 17S position. In contrast, nsec1, another synaptosomal protein, migrated to the 4.3S position as previously observed (Pevsner, *et al.*, 1994b). This result indicates that all of the soluble rsec6 and rsec8 protein is in a large complex and that little or no protein is found in monomeric state.

Because the Coomassie blue-stained glycerol gradient protein profile (Figure 1A) showed the presence of many proteins in the 17S region, it was necessary to determine whether the co-fractionating rsec6 and rsec8 were in the same complex.

To address this question, rsec6 and rsec8 were immunoprecipitated from polyethylene glycol-fractionated rat brain supernatant with affinity-purified antibodies against rsec8 or with control rabbit immunoglobulin. The immunoprecipitated sample was analyzed for the presence of rsec6, rsec8 and nsec1 by Western blotting.

The results are shown in Figure 1C. Brain is the starting material; Ab represents proteins bound to the anti-rsec8 antibody in the absence of brain homogenate; Ab + brain represents proteins bound to the anti-rsec8 antibody following incubation with brain homogenate; and Ig + brain represents proteins bound to the control rabbit immunoglobulin following incubation with brain homogenate. The results show that rsec6, but not nsec1, co-immunoprecipitated with rsec8 from soluble brain proteins using affinity-purified rabbit polyclonal anti-rsec8 antibodies. No rsec6, rsec8

or nsec1 were immunoprecipitated by control rabbit immunoglobulin, confirming the specific binding of the SA-17S complex to anti-rsec8 antibodies. These data demonstrate that both rsec6 and rsec8 are components of the same high molecular weight complex.

EXAMPLE 2

Purification of the Mammalian SA-17S Complex

The SA-17S complex was purified from frozen rat brain by four sequential column chromatographic steps to define other members of the complex. Figure 2A shows a Coomassie blue-stained SDS polyacrylamide gel analysis of pooled column fractions. Abbreviations are as follows: Lys, starting soluble brain proteins; HT, hydroxyapatite eluant; TMAE, TMAE anion exchanger eluant; GF, HW55S gel filtration eluant; TMAE2, second TMAE anion exchanger eluant. Positions of rsec6 and rsec8 on the gel are indicated on the right as 6 and 8, respectively. Fifteen μg of proteins were loaded in lane Lys, HT and TMAE; eight μg of proteins were loaded in lane GF; and three μg of proteins were loaded in lane TMAE2.

The enrichment of the SA-17S complex following each chromatographic step was monitored by Western blot analysis using mouse polyclonal antibodies against rsec6 and rsec8, as shown in Figure 2B. Initially, cytosol prepared from frozen rat brains was applied to and step-eluted from hydroxyapatite. No significant amount of rsec6 and rsec8 was detected in the flow-through from this column. The pooled hydroxyapatite eluant exhibiting an enrichment of rsec6 and rsec8 immunoreactivity was concentrated and further purified using a strongly basic anion exchange resin, TMAE-Fractogel. All rsec6 and rsec8 immunoreactivity was retained by the resin and was eluted by a linear salt gradient. Next, taking advantage of the large size of the complex, the TMAE eluant was further fractionated by HW55-S gel filtration chromatography. The rsec6 and rsec8 immunoreactivity was eluted in a single peak with an apparent native molecular weight of 650 - 700 kDa. At this stage of purification, eight polypeptides of molecular weights between 70 kDa and 110 kDa were visible on a SDS polyacrylamide gel stained with Coomassie blue (Figure 2A).

The last stage of purification involved a second anion exchange chromatography utilizing TMAE-Fractogel. Analysis of salt-eluted fractions from this column by SDS-PAGE revealed that elution of eight distinct proteins with molecular weights ranging from 71 kDa to 110 kDa (Figure 2C) coincided exactly with the elution of rsec6 and rsec8 immunoreactivity. SDS-PAGE analysis of pooled peak rsec6 and rsec8 immunoreactivity fractions indicated that these same eight proteins constituted at least 95% of the total proteins in this fraction (Figure 2A, lane TMAE2; Figure 2C).

Fractionation of the purified complex on a glycerol gradient demonstrated that all eight components co-migrate at the 17S position. In addition, all eight proteins co-immunoprecipitated with rsec8 monoclonal antibodies. Approximately 100-200 μg of SA-17S complex was recovered from 50 rat brains after purification. Quantitation of the enrichment of the SA-17S complex by Western blot using ^{125}I-labeled secondary antibodies suggests that the complex constitutes approximately 0.1% of the total soluble brain protein. All eight proteins were approximately equally stained by Coomassie blue (although p79 reproducibly appears to stain somewhat less intensely) suggesting a stoichiometry of one copy of each protein within the complex (Figure 2C). This 1:1 stoichiometry is further supported by the apparent molecular weight of 600-700 kDa of the native complex. Peptide sequences from protein bands of 110 kDa and 86 kDa indicate that they are rsec8 and rsec6, respectively.

EXAMPLE 3

Peptide Sequencing of the SA-17S Complex Components

To further characterize individual components of the mammalian SA-17S complex, the purified complex was fractionated on an SDS polyacrylamide gel and each polypeptide band was cut out and individually subjected to in-gel proteolysis with trypsin, Lys C and/or Glu C. The digested peptides were eluted from the gel, fractionated by high performance liquid chromatography (HPLC), and in many cases, analyzed by mass spectrometry for peptide purity and mass.

Figures 3A, 3B, 3C and 3D show the mass spectrometric analyzes of HPLC peptide peaks from four proteins, p102, p96, p84 and p71, respectively. A single peptide peak in the mass spectrometry profile suggests the presence of one peptide species in the analyzed HPLC peptide peak, as shown in Figs. 3A, 3B, 3C and 3D. The multiple peaks shown in Fig. 3D are due to the binding of different amounts of salt to the peptide (amino acid sequence analysis of this peptide peak confirmed the presence of only one peptide species). The mass of each peptide predicted by mass spectrometry is shown above the peptide peak. The amino acid sequence of each peptide determined by peptide sequencing and its mass (protonated form of peptide) calculated from the determined peptide sequence is shown beside corresponding peptide peak, along with its SEQ ID NO. In Panels A to C the calculated and observed masses matched with less than 0.1% difference.

Figures 4A-H, as well as Tables 1-8 below, show all the peptide sequences obtained from the eight predicted members of the SA-17S complex. Protein components of purified SA-17S complex were digested with a combination Trypsin (cuts after a lysine or an arginine residue), Lys C (cuts after a lysine residue) and/or Glu C (cuts after a glutamic acid) as described in the

Experimental Procedures. p110 or rsec8 peptides were obtained from a combination of Lys C and Trypsin digestion; p106 peptides 1-6 were obtained from a combination of Lys C and Trypsin digestion and p106 peptides 7-8 were obtained from Lys C digestion; p102 peptides 1-4 were obtained from a combination of Lys C and trypsin digestion and p102 peptides 5-7 were obtained from Lys C digestion; p96 peptides 1-3 were obtained from Lys C digestion and p96 peptides 4-6 were obtained from a combination of Lys C and Glu C digestion; p86 or rsec6 peptide 1 was obtained from Lys C digestion and p86 or rsec6 peptides 2-3 were obtained from a combination of Lys C and Glu C digestion; p84 peptide 1 was obtained from Lys C digestion and p84 peptides 2-9 were obtained from a combination of Lys C and Glu C digestion; p79 peptides 1-6 were obtained from Lys C digestion and p79 peptides 7-10 were obtained from a combination of Lys C and Glu C digestion; p71 peptides were obtained from Lys C digestion.

Table 1 - rsec6

Name	SEQ ID NO:	Sequence
rsec6 .1	5	DFRQSINTIEXL
rsec6 .2	6	QGPSQASPNYXP
rsec6 .3	7	AAIQSQLDGVRTGLSQ

Table 2 - rsec8

Name	SEQ ID NO:	Sequence
rsec8.1	8	XAPEGPLIDVXNI
rsec8.2	9	EFAAFFAK
rsec8.3	10	XLGVQRPLLQSTSIXE

Table 3 - SA-17S p71

Name	SEQ ID NO:	Sequence
p71.1	11	XNQVAFQHFQELDEHI
p71.2	12	VCHLXDQLEXVN
p71.3	13	LHLIAQELPFDRFSEVK

Table 4 - SA-17S p79

Name	SEQ ID NO:	Sequence
p79.1	14	XTDYIAE
p79.2	15	ETYGAFLSRSXG
p79.3	16	XXPPQGVPYNPASP
p79.4	17	XXQEEETLMFIRGN
p79.5	18	ALFIRDDXQF
p79.6	19	NLPVFQSCL
p79.7	20	AVEYFQDKFPD
p79.8	21	YRVEQVGDMIDRLFDTS
p79.9	22	VYEDPALSAIFLHNNYNY
p79.10	23	XXYGAFLHRYSSVPFVYGXH

Table 5 - SA-17S p84

Name	SEQ ID NO:	Sequence
p84.1	24	QLSQQSDGDRDLQEWRQRVQALAEETAQYK
p84.2	25	XLQLSFNFSEPNRQRP
p84.3	26	SIPLALLPAAAAGA
p84.4	27	DAVXQNSTQAAETEN
p84.5	28	DYRNDEA
p84.6	29	ENNPEEDDPS
p84.7	30	XLSQQSDXG
p84.8	31	AAALRAPPXVTS
p84.9	32	XKREPLE

Table 6 - SA-17S p96

Name	SEQ ID NO:	Sequence
p96.1	33	VVGQFPFQDTELEK
p96.2	34	XVYEIFDN
p96.3	35	DFLESIR
p96.4	36	XDQDLQLADYDHMT
p96.5	37	STNLLLTRTLXN

Table 7 - SA-17S p102

Name	SEQ ID NO:	Sequence
p102.1	38	YLSGLQAPGXPASQSIGAQ
p102.2	39	GGLSTFFEAQDALSAIHQK
p102.3	40	ASNTADTXRQER
p102.4	41	XRENYIEGGI
p102.5	42	ENLGRLFENYI
p102.6	43	XDYDVVINDYE
p102.7	44	XIPXLSTRPANP

Table 8 - SA-17S p106

Name	SEQ ID NO:	Sequence
p106.1	45	XXYGEIAXK
p106.2	46	XATVSLPEK
p106.3	47	XDYGVIAND
p106.4	48	LIKYFFMVASVK
p106.5	49	ELPEFNLHFFK
p106.6	50	XLQDVDLASXR
p106.7	51	XNRXNEPAVNVL
p106.8	52	XQLXNIVEPEXIY

"X" represents residues whose identity has not been unambiguously determined.

As mentioned above, peptide sequences from p110 and p86 confirmed that these two proteins are rsec8 and rsec6 respectively. Furthermore, all of the peptide sequences from these two protein bands match the amino acid sequence predicted by rsec6 and rsec8 cDNAs demonstrating that the bands are free of contaminating proteins and that the SA-17S complex is substantially pure or substantially purified.

Comparison of remaining peptide sequences to "GENBANK" and a database of human expressed sequence tag (EST) cDNAs generated by the Institute for Genomic Research (TIGR) found matches to two proteins (p71 and p79). Overall, the amino acid sequences match the sequences predicted from the cDNAs with an accuracy greater than 97%. Taken together, these results suggest that members of the SA-17S complex are novel proteins which have not been previously characterized.

EXAMPLE 4

Expression Pattern of the SA-17S Complex

To determine the site of SA-17S complex function in brain, the brain regional distribution of these proteins was examined using SDS-PAGE/Western blot analyzes as described above (10 μg of proteins loaded per lane). Figure 5A shows that rsec8 is expressed in all regions of rat brain examined and there is no significant brain regional variation. A similar expression pattern is also observed for rsec6, suggesting that both proteins are required by all brain cells.

To determine whether the SA-17S complex functions in multiple exocytotic pathways in addition to the regulated pathway underlying neurotransmission, the presence of rsec8 in cell lines derived from kidney, ovary, pituitary and adrenal medulla tissues was investigated with SDS-PAGE/Western blot analyzes as described above. The results are shown in Figure 5B. Affinity-purified anti-rsec8 rabbit polyclonal antibodies detected rsec8 as a 110 kDa protein in all the cell lines examined. rsec6 was also observed in all cell lines examined. The cells with the highest amounts of rsec8 were AtT-20 and PC-12 cells. Both of these cell lines have regulated secretory pathways and contain numerous secretory vesicles as well as synaptic proteins, indicating that the expression of the SA-17S complex may parallel the level of secretory activity in cells.

EXAMPLE 5

Subcellular Localization of the SA-17S Complex

Cell fractionation studies were carried out to determine the solubility properties of the SA-17S complex. Rat brain homogenate was subjected to a 1,000 xg spin to yield postnuclear supernatant

(PNS). The PNS was then subjected to either (i) a 100,000 xg spin to yield soluble (PNS sup) and membrane protein (PNS pellet) fractions or (ii) a 25,000 xg spin to yield a supernatant and a crude synaptosomal pellet (crude synaptosomes). The synaptosomal pellet was lysed in 2 mM Hepes, pH 7.4 and homogenized with a Polytron. The homogenate was then subjected to a 100,000 xg spin to yield both soluble (cytosol) and membrane (memb) fractions. The membrane pellets were resuspended in 20 mM Hepes, pH 7.4 to volumes equal to that of the corresponding supernatants. Five μl of each protein sample was loaded per lane.

Figure 6A shows results of a Western blot analysis for the presence of rsec6 and rsec8 in the subcellular fractionation of the SA-17S complex. Upon homogenization of freshly dissected rat brain, rsec6 and rsec8 were present in both soluble and insoluble fractions. Approximately 25% and 75% of rsec6 and rsec8 were found in the supernatant and the membrane pellet respectively. Similarly, in crude synaptosomes, the majority of rsec6 and rsec8 was found associated with synaptosomal membranes. Very little rsec6 and rsec8 were found in the synaptosomal cytosol. However, in frozen brain more rsec6 and rsec8 (approximately 50%) was found in the soluble fraction. The presence of rsec6 and rsec8 in the membrane fraction was not due to the entrapment of the complex in intact cells or organelles in the postnuclear supernatant because the distribution of these two proteins was similar when rat brain was completely homogenized in hypotonic buffer with a Polytron. Likewise, the presence of these two proteins in the supernatant was not due to contaminating membrane fragments because both SV2, a synaptic vesicle marker, and Na/K ATPase, a plasma membrane marker, were detected only in synaptosomal membrane pellet and not in synaptosomal cytosol.

To determine if the pool of the SA-17S complex that pelleted with crude synaptosomal membranes at 100,000 xg was due to its association with synaptosomal membranes or with large proteinaceous aggregates, crude synaptosomal membranes were subjected to sucrose gradient flotation. Crude synaptosomal membranes were placed at the bottom of a sucrose gradient and allowed to float up into the gradient. The flotation of the SA-17S complex into the gradient was monitored by Western blot analysis using mouse polyclonal antibodies. The migration of plasma membrane and synaptic vesicles was also monitored using rabbit polyclonal antibodies against Na/K ATPase and a monoclonal antibody against synaptophysin respectively. Fraction 1 corresponds to the top of the gradient.

The results are shown in Figure 6B. Both rsec6 and rsec8 floated up into the sucrose gradient, as observed with both Na/K ATPase, and synaptophysin (a synaptic vesicle marker). Very little rsec6 and rsec8 were detected at the bottom of the gradient as protein aggregates. These data

suggest that the insoluble pool of SA-17S complex is associated with synaptosomal (brain) membranes.

To investigate the nature of SA-17S complex association with membranes, brain membranes were extracted with 20 mM Tris buffer, 1.5 M NaCl, 4% Triton X-100, or 4 M urea. The extracted membranes were centrifuged and the resulting supernatants and membrane pellets were subjected to Western blot analyzes. Lysed brain membranes were extracted with either 20 mM Tris, pH 8.0, 1.5 M NaCl, 4% Triton X-100 or 4 M urea. Following extraction, the membranes were centrifuged to yield soluble (s) and membrane (p) fractions. The presence of rsec8 in these fractions was detected and quantitated by phosphorimaging using anti-rsec8 primary and ^{125}I-labeled secondary antibodies (see Materials and Methods, above).

The results are shown in Fig. 6C. Approximately 4%, 46%, 60% and 88% of the SA-17S complex were extracted by Tris buffer, 1.5 M NaCl, 4% Triton X-100 and 4 M urea, respectively. The incomplete extraction of the SA-17S complex in the presence of a high concentration of salt suggests that this complex may bind very tightly to the membranes. Interestingly, a fraction of the native SA-17S complex is found in the Triton X-100 insoluble pellet following membrane solubilization, contrary to the observation that purified soluble SA-17S complex is completely soluble in Triton X-100, suggesting that the membrane-bound complex may be associated with cytoskeletal elements. Taken together, these observations suggest that the insoluble pool of SA-17S complex may be associated with cytoskeletal elements which, in turn, bind to membranes.

Since rsec6 and rsec8 floated to the same region of the sucrose gradient as synaptic vesicles and plasma membranes, the possibility of an association between the SA-17S complex and synaptic vesicles was investigated. Synaptic vesicles were immunoprecipitated using an anti-SV2 (a synaptic vesicle-specific integral membrane protein) monoclonal antibody, or control mouse immunoglobulin, coupled to Dynabeads M-500. The immunoprecipitated vesicles were examined for the presence of synaptotagmin and rsec8 by Western blotting.

Figure 6D shows one such Western blot analysis. While the synaptic vesicle-specific protein synaptotagmin was present in anti-SV2 antibody immunoprecipitated vesicles, no rsec8 was detected even upon longer exposure. Neither protein was immunoprecipitated by control mouse immunoglobulin indicating a specific association of synaptic vesicles with anti-SV2 antibody. These results suggest that SA-17S complex is not associated strongly or stably with synaptic vesicles leaving the plasma membrane as the likely site of its membrane localization.

EXAMPLE 6

Localization of rsec8 in Cultured Hippocampal Neurons

To confirm the presence of the SA-17S complex in synapses, its localization in primary hippocampal cultures was studied by immunofluorescence microscopy. Fifteen to twenty day-old cultures of primary hippocampal neurons were fixed and immunostained with antibodies against rsec8 (Figs. 7A and 7B) and synaptotagmin (Fig. 7C). Fig. 7D shows a larger magnification of rsec8 staining overlaid with that of synaptotagmin at two synaptic terminals indicated by arrows. Synaptic terminals in these cultures were identified by the presence of the synaptic vesicle marker, synaptotagmin. Bar = 7μm.

Figure 7A shows that rsec8 labeling was detected throughout hippocampal neurons, including the cell bodies, dendrites, axons and nerve terminals. Brighter rsec8 staining at synapses suggests an accumulation of the SA-17S complex in nerve terminals (Figs. 7A and B). Although both synaptotagmin and rsec8 were detected in synaptic terminals, staining of rsec8 was more concentrated near the plasma membrane than that of synaptotagmin (Figs. 7B, 7C and 7D). Many terminals displayed rsec8 labeling in peripheral areas where it did not co-localize with the more centrally positioned synaptotagmin staining.

Glial and other non-neural cells in the hippocampal neuron cultures were also stained, although typically more weakly than the neurons. As controls, pre-immune immunoglobulins of same protein concentrations as the anti-rsec8 antibodies were used as the primary antibodies. At the same time exposures, no staining was observed in these neurons using identical labeling procedures. Taken together, these biochemical and histochemical data suggest that the SA-17S complex is localized to the plasma membrane.

EXAMPLE 7

Co-immunoprecipitation of rsec8 Complex with Syntaxin

Monoclonal antibodies were generated against rsec8 to study the properties of the SA-17S complex, including its membrane association in brain. The specificity of seven monoclonal antibodies generated against rsec8 was investigated by Western blot analysis as described above (ten μg of brain postnuclear supernatant were loaded per lane). As shown in Figure 8A, all these antibodies (with the exception of mAb15E12) recognized a single band of 110 kDa in the brain postnuclear supernatant. Monoclonal antibody 15E12 detected a major band of 110 kDa in addition to two minor bands of 65 kDa and 90 kDa. These two lower molecular weight bands are likely to be degradation products of rsec8.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Scheller, Richard H.

(ii) TITLE OF INVENTION: Methods and Compositions for Modulation of Vesicular Release

(iii) NUMBER OF SEQUENCES: 62

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Dehlinger & Associates
(B) STREET: 350 Cambridge Avenue, Suite 250
(C) CITY: Palo Alto
(D) STATE: CA
(E) COUNTRY: USA
(F) ZIP: 94306

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Diskette
(B) COMPUTER: IBM Compatible
(C) OPERATING SYSTEM: DOS
(D) SOFTWARE: FastSEQ for Windows Version 2.0

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER: To be assigned
(B) FILING DATE: 19-DEC-1997
(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA
(A) APPLICATION NUMBER: 60/033,905
(B) FILING DATE: 20-DEC-1996

(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Dehlinger, Peter J.
(B) REGISTRATION NUMBER: 28,006
(C) REFERENCE/DOCKET NUMBER: 8600-0179.30

(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: (650) 324-0880
(B) TELEFAX: (650) 324-0960

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2265 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: rsec6

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 1..2265

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

```
ATG TGC AAA GAT TCT GCC TGC TTT TCG ACT ATG AAG GAG ACA GAC CTG
48
Met Cys Lys Asp Ser Ala Cys Phe Ser Thr Met Lys Glu Thr Asp Leu
 1               5                  10                  15

GAG GCT GTT GCA ACA GCA GTC CAA AGG GTG GCT GGG ATG CTT CAG CGC
96
Glu Ala Val Ala Thr Ala Val Gln Arg Val Ala Gly Met Leu Gln Arg
            20                  25                  30

CCA GAC CAG CTG GAC AAA GTG GAG CAG TAT CGC AGA AGG GAG GCT CGG      144
Pro Asp Gln Leu Asp Lys Val Glu Gln Tyr Arg Arg Arg Glu Ala Arg
        35                  40                  45

AAG AAG GCC TCT GTG GAG GCC AGG CTA AAG GCC GCA ATC CAG TCT CAA      192
Lys Lys Ala Ser Val Glu Ala Arg Leu Lys Ala Ala Ile Gln Ser Gln
    50                  55                  60

CTA GAT GGC GTC CGC ACA GGC CTA AGC CAA CTG CAC AAT GCA CTG AAT      240
Leu Asp Gly Val Arg Thr Gly Leu Ser Gln Leu His Asn Ala Leu Asn
65                  70                  75                  80
```

GAT GTC AAG GAT ATC CAG CAG TCA CTG GCT GAT GTG AGC AAG GAC TGG 288
Asp Val Lys Asp Ile Gln Gln Ser Leu Ala Asp Val Ser Lys Asp Trp
85 90 95

AGG CAG AGC ATC AAC ACC ATC GAG AGT CTC AAG GAC GTA AAA GAC GCA 336
Arg Gln Ser Ile Asn Thr Ile Glu Ser Leu Lys Asp Val Lys Asp Ala
100 105 110

GTG GTG CAG CAC AGC CAG CTG GCT GCA GCT GTG GAG AAC CTC AAG AAC 384
Val Val Gln His Ser Gln Leu Ala Ala Ala Val Glu Asn Leu Lys Asn
115 120 125

ATA TTC TCT GTG CCT GAG ATT GTG AGG GAG ACC CAA GAT CTC ATC GAG 432
Ile Phe Ser Val Pro Glu Ile Val Arg Glu Thr Gln Asp Leu Ile Glu
130 135 140

CAA GGG GCT CTC CTG CAG GCC CAC CGG AAG CTA ATG GAT CTG GAG TGC 480
Gln Gly Ala Leu Leu Gln Ala His Arg Lys Leu Met Asp Leu Glu Cys
145 150 155 160

TCC CGG GAT GGG CTA ATG TGT GAG CAG TAC CGC ATG GAC AGT GGG AAC 528
Ser Arg Asp Gly Leu Met Cys Glu Gln Tyr Arg Met Asp Ser Gly Asn
165 170 175

AAA CGG GAC ATG ACC CTC ATT CAT GGC TAC TTC GGT AGC ACA CAG GGG 576
Lys Arg Asp Met Thr Leu Ile His Gly Tyr Phe Gly Ser Thr Gln Gly
180 185 190

CTC TCT GAC GAG CTG GCC AAG CAG CTG TGG ATG GTG CTG CAA AGA TCG 624
Leu Ser Asp Glu Leu Ala Lys Gln Leu Trp Met Val Leu Gln Arg Ser
195 200 205

CTG GTC ACT GTC CGC CGG GAT CCC ACC TTG CTG GTC TCC GTG GTC AGG 672
Leu Val Thr Val Arg Arg Asp Pro Thr Leu Leu Val Ser Val Val Arg
210 215 220

ATC ATT GAA AGG GAA GAA AAA ATT GAC AGG CGG ATA CTT GAT CGA AAA 720
Ile Ile Glu Arg Glu Glu Lys Ile Asp Arg Arg Ile Leu Asp Arg Lys
225 230 235 240

AAG CAA ACT GGG TTT GTT CCT CCT GGA AGG CCC AAA AAC TGG AAG GAA 768
Lys Gln Thr Gly Phe Val Pro Pro Gly Arg Pro Lys Asn Trp Lys Glu
245 250 255

AAA ATG TTT GCC GTC TTG GAC AGA ACT GTG ACG ACT AGA ATC GAA GGC 816
Lys Met Phe Ala Val Leu Asp Arg Thr Val Thr Thr Arg Ile Glu Gly
260 265 270

ACG CAG GCG GAC ACC AGA GAA TCT GAC AAG ATG TGG CTC GTG CGC CAC 864
Thr Gln Ala Asp Thr Arg Glu Ser Asp Lys Met Trp Leu Val Arg His
275 280 285

CTG GAG ATC ATT AGG AAG TAC GTC CTG GAT GAC CTC GTC ATC GCC AAG 912
Leu Glu Ile Ile Arg Lys Tyr Val Leu Asp Asp Leu Val Ile Ala Lys
290 295 300

AAC CTG CTG GTG CAG TGC TTC CCT CCT CAC TAT GAC ATC TTT AAG AAC 960
Asn Leu Leu Val Gln Cys Phe Pro Pro His Tyr Asp Ile Phe Lys Asn
305 310 315 320

CTC CTG AGC ATG TAC CAC CAG GCC TTG AGC ATT CGG ATG CAG GAC CTC 1008
Leu Leu Ser Met Tyr His Gln Ala Leu Ser Ile Arg Met Gln Asp Leu
325 330 335

GCC TCA GAG GAC CTT GAG GCC AAC GAG ATT GTG AGC CTC TTG ACC TGG 1056
Ala Ser Glu Asp Leu Glu Ala Asn Glu Ile Val Ser Leu Leu Thr Trp
340 345 350

GTC CTA AAT ACC TAC ACC AGT GCA GAG ATG ATG GGG AAT GTG GAG CTG 1104
Val Leu Asn Thr Tyr Thr Ser Ala Glu Met Met Gly Asn Val Glu Leu
355 360 365

GCC CCA GAG GTG GAC GTT AAT GCC CTG GAA CCG CTC CTC TCA CCA AAC 1152
Ala Pro Glu Val Asp Val Asn Ala Leu Glu Pro Leu Leu Ser Pro Asn
370 375 380

GTG GTC TCT GAG CTG CTC GAC ACA TAC ATG TCA ACA CTC ACG TCC AAC 1200
Val Val Ser Glu Leu Leu Asp Thr Tyr Met Ser Thr Leu Thr Ser Asn
385 390 395 400

ATC ATT GCC TGG CTT CGG AAA GCA CTG GAG ACA GAC AAG AAA GAC TGG 1248
Ile Ile Ala Trp Leu Arg Lys Ala Leu Glu Thr Asp Lys Lys Asp Trp
405 410 415

AGC AAA GAG ACG GAG CCG GAA GCA GAC CAG GAC GGC TAT TAT CAG ACG 1296
Ser Lys Glu Thr Glu Pro Glu Ala Asp Gln Asp Gly Tyr Tyr Gln Thr
420 425 430

ACA CTT CCT GCC ATT GTA TTC CAG ATG TTT GAA CAG AAT CTT CAA GTT 1344
Thr Leu Pro Ala Ile Val Phe Gln Met Phe Glu Gln Asn Leu Gln Val
435 440 445

GCT GCT CAA ATA AGT GAA GAT TTG AAA ACA AAG GTA TTA GTT TTG TGT 1392
Ala Ala Gln Ile Ser Glu Asp Leu Lys Thr Lys Val Leu Val Leu Cys
450 455 460

CTT CAG CAA ATG AAT TCT TTC CTA AGT AGA TAC AAA GAG GAA GCC CAG 1440
Leu Gln Gln Met Asn Ser Phe Leu Ser Arg Tyr Lys Glu Glu Ala Gln
465 470 475 480

CTT TAC AAA GAG GAG CAC CTG AGA AAC CGG CAG CAC CCA CAC TGT TAC 1488
Leu Tyr Lys Glu Glu His Leu Arg Asn Arg Gln His Pro His Cys Tyr
485 490 495

GTG CAG TAC ATG GTC GCC ATC ATC AAT AAC TGC CAG ACC TTC AAA GAA 1536
Val Gln Tyr Met Val Ala Ile Ile Asn Asn Cys Gln Thr Phe Lys Glu
500 505 510

TCC ATC ATC AGT CTG AAA AGA AAA TAC CTA AAA CCC GAA ACA GAG GAA 1584
Ser Ile Ile Ser Leu Lys Arg Lys Tyr Leu Lys Pro Glu Thr Glu Glu
515 520 525

AGC CTG TGT CAG AGT CAG CCC AGC ATG GAT GGG ATT CTA GAT GCC ATT 1632
Ser Leu Cys Gln Ser Gln Pro Ser Met Asp Gly Ile Leu Asp Ala Ile
530 535 540

GCT AAG GAA GGC TGC AGC AGT CTG CTA GAG GAG GTC TTC CTG GAT CTA 1680
Ala Lys Glu Gly Cys Ser Ser Leu Leu Glu Glu Val Phe Leu Asp Leu
545 550 555 560

GAG CAA CAT CTG AAT GAG CTA ATG ACA AAG AAG TGG ATG TTA GGA TCA 1728
Glu Gln His Leu Asn Glu Leu Met Thr Lys Lys Trp Met Leu Gly Ser
565 570 575

AAT GCT GTG GAC ATC ATC TGT GTC ACC GTA GAA GAC TAC TTC AAT GAC 1776
Asn Ala Val Asp Ile Ile Cys Val Thr Val Glu Asp Tyr Phe Asn Asp
580 585 590

TTC GCC AAA ATT AAA AAG CCA TAC AAA AAG AGG ATG ACA GCT GAG GCA 1824
Phe Ala Lys Ile Lys Lys Pro Tyr Lys Lys Arg Met Thr Ala Glu Ala
595 600 605

(A) LENGTH: 755 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

```
Met Cys Lys Asp Ser Ala Cys Phe Ser Thr Met Lys Glu Thr Asp Leu
 1               5                  10                  15

Glu Ala Val Ala Thr Ala Val Gln Arg Val Ala Gly Met Leu Gln Arg
            20                  25                  30

Pro Asp Gln Leu Asp Lys Val Glu Gln Tyr Arg Arg Arg Glu Ala Arg
        35                  40                  45

Lys Lys Ala Ser Val Glu Ala Arg Leu Lys Ala Ala Ile Gln Ser Gln
    50                  55                  60

Leu Asp Gly Val Arg Thr Gly Leu Ser Gln Leu His Asn Ala Leu Asn
65                  70                  75                  80

Asp Val Lys Asp Ile Gln Gln Ser Leu Ala Asp Val Ser Lys Asp Trp
                85                  90                  95

Arg Gln Ser Ile Asn Thr Ile Glu Ser Leu Lys Asp Val Lys Asp Ala
            100                 105                 110

Val Val Gln His Ser Gln Leu Ala Ala Ala Val Glu Asn Leu Lys Asn
        115                 120                 125

Ile Phe Ser Val Pro Glu Ile Val Arg Glu Thr Gln Asp Leu Ile Glu
    130                 135                 140

Gln Gly Ala Leu Leu Gln Ala His Arg Lys Leu Met Asp Leu Glu Cys
145                 150                 155                 160

Ser Arg Asp Gly Leu Met Cys Glu Gln Tyr Arg Met Asp Ser Gly Asn
                165                 170                 175

Lys Arg Asp Met Thr Leu Ile His Gly Tyr Phe Gly Ser Thr Gln Gly
            180                 185                 190

Leu Ser Asp Glu Leu Ala Lys Gln Leu Trp Met Val Leu Gln Arg Ser
```

195 200 205

Leu Val Thr Val Arg Arg Asp Pro Thr Leu Leu Val Ser Val Val Arg
210 215 220

Ile Ile Glu Arg Glu Glu Lys Ile Asp Arg Arg Ile Leu Asp Arg Lys
225 230 235 240

Lys Gln Thr Gly Phe Val Pro Pro Gly Arg Pro Lys Asn Trp Lys Glu
245 250 255

Lys Met Phe Ala Val Leu Asp Arg Thr Val Thr Thr Arg Ile Glu Gly
260 265 270

Thr Gln Ala Asp Thr Arg Glu Ser Asp Lys Met Trp Leu Val Arg His
275 280 285

Leu Glu Ile Ile Arg Lys Tyr Val Leu Asp Asp Leu Val Ile Ala Lys
290 295 300

Asn Leu Leu Val Gln Cys Phe Pro Pro His Tyr Asp Ile Phe Lys Asn
305 310 315 320

Leu Leu Ser Met Tyr His Gln Ala Leu Ser Ile Arg Met Gln Asp Leu
325 330 335

Ala Ser Glu Asp Leu Glu Ala Asn Glu Ile Val Ser Leu Leu Thr Trp
340 345 350

Val Leu Asn Thr Tyr Thr Ser Ala Glu Met Met Gly Asn Val Glu Leu
355 360 365

Ala Pro Glu Val Asp Val Asn Ala Leu Glu Pro Leu Leu Ser Pro Asn
370 375 380

Val Val Ser Glu Leu Leu Asp Thr Tyr Met Ser Thr Leu Thr Ser Asn
385 390 395 400

Ile Ile Ala Trp Leu Arg Lys Ala Leu Glu Thr Asp Lys Lys Asp Trp
405 410 415

Ser Lys Glu Thr Glu Pro Glu Ala Asp Gln Asp Gly Tyr Tyr Gln Thr
420 425 430

Thr Leu Pro Ala Ile Val Phe Gln Met Phe Glu Gln Asn Leu Gln Val

435 440 445

Ala Ala Gln Ile Ser Glu Asp Leu Lys Thr Lys Val Leu Val Leu Cys
450 455 460

Leu Gln Gln Met Asn Ser Phe Leu Ser Arg Tyr Lys Glu Glu Ala Gln
465 470 475 480

Leu Tyr Lys Glu Glu His Leu Arg Asn Arg Gln His Pro His Cys Tyr
485 490 495

Val Gln Tyr Met Val Ala Ile Ile Asn Asn Cys Gln Thr Phe Lys Glu
500 505 510

Ser Ile Ile Ser Leu Lys Arg Lys Tyr Leu Lys Pro Glu Thr Glu Glu
515 520 525

Ser Leu Cys Gln Ser Gln Pro Ser Met Asp Gly Ile Leu Asp Ala Ile
530 535 540

Ala Lys Glu Gly Cys Ser Ser Leu Leu Glu Glu Val Phe Leu Asp Leu
545 550 555 560

Glu Gln His Leu Asn Glu Leu Met Thr Lys Lys Trp Met Leu Gly Ser
565 570 575

Asn Ala Val Asp Ile Ile Cys Val Thr Val Glu Asp Tyr Phe Asn Asp
580 585 590

Phe Ala Lys Ile Lys Lys Pro Tyr Lys Lys Arg Met Thr Ala Glu Ala
595 600 605

His Arg Arg Val Val Val Glu Tyr Leu Arg Ala Val Met Gln Lys Arg
610 615 620

Ile Ser Phe Arg Ser Ala Glu Glu Arg Lys Glu Gly Ala Glu Lys Met
625 630 635 640

Val Arg Glu Ala Glu Gln Leu Arg Phe Leu Phe Arg Lys Leu Ala Ser
645 650 655

Gly Phe Gly Glu Asp Ala Asp Gly His Cys Asp Thr Ile Val Ala Val
660 665 670

Ala Glu Val Ile Lys Leu Thr Asp Pro Ser Leu Leu Tyr Leu Glu Val

675 680 685

Ser Thr Leu Val Ser Lys Tyr Pro Asp Ile Arg Asp Asp His Ile Gly
690 695 700

Ala Leu Leu Ala Leu Arg Gly Asp Ala Ser Arg Asp Met Lys Gln Thr
705 710 715 720

Ile Met Glu Thr Leu Glu Gln Gly Pro Met Gln Ala Ser Pro Asn Tyr
725 730 735

Val Pro Ile Phe Gln Glu Ile Val Val Pro Ser Leu Asn Val Ala Lys
740 745 750

Leu Leu Lys
755

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2925 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: double
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: rsec8

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 1..2925

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

ATG GCG GCA GAA GCA GCT GGT GGG AAA TAC AGG AGC ACA GTC AGC AAA
48
Met Ala Ala Glu Ala Ala Gly Gly Lys Tyr Arg Ser Thr Val Ser Lys

46

1 5 10 15

AGC AAA GAC CCC TCG GGG CTG CTC ATC TCG GTG ATC AGG ACT CTG TCT
96
Ser Lys Asp Pro Ser Gly Leu Leu Ile Ser Val Ile Arg Thr Leu Ser
20 25 30

ACC AGT GAT GAT GTT GAA GAC CGA GAA AAT GAG AAA GGT CGC CTT GAA 144
Thr Ser Asp Asp Val Glu Asp Arg Glu Asn Glu Lys Gly Arg Leu Glu
35 40 45

GAA GCC TAT GAG AAG TGT GAC CGT GAC CTG GAT GAA TTG ATC GTT CAG 192
Glu Ala Tyr Glu Lys Cys Asp Arg Asp Leu Asp Glu Leu Ile Val Gln
50 55 60

CAC TAC ACA GAA TTG ACA ACA GCC ATT CGC ACA TAC CAG AGC ATC ACA 240
His Tyr Thr Glu Leu Thr Thr Ala Ile Arg Thr Tyr Gln Ser Ile Thr
65 70 75 80

GAA CGC ATC ACT AAC TCC AGG AAT AAA ATC AAG CAG GTA AAA GAG AAC 288
Glu Arg Ile Thr Asn Ser Arg Asn Lys Ile Lys Gln Val Lys Glu Asn
85 90 95

CTG CTT TCC TGC AAG ATG CTG TTG CAT TGC AAA CGG GAT GAG CTT CGT 336
Leu Leu Ser Cys Lys Met Leu Leu His Cys Lys Arg Asp Glu Leu Arg
100 105 110

AAA CTA TGG ATT GAA GGA ATT GAG CAT AAG CAT GTC CTG AAC CTT CTG 384
Lys Leu Trp Ile Glu Gly Ile Glu His Lys His Val Leu Asn Leu Leu
115 120 125

GAT GAG ATT GAA AAC ATC AAG CAA GTG CCT CAA AAG CTG GAA CAG TGC 432
Asp Glu Ile Glu Asn Ile Lys Gln Val Pro Gln Lys Leu Glu Gln Cys
130 135 140

ATG GCC AGC AAG CAC TAC CTC AGC GCC ACG GAC ATG CTG GTG TCA GCA 480
Met Ala Ser Lys His Tyr Leu Ser Ala Thr Asp Met Leu Val Ser Ala
145 150 155 160

GTG GAG TCT CTG GAG GGT CCG CTG CTC CAG GTG GAA GGA CTC AGT GAC 528
Val Glu Ser Leu Glu Gly Pro Leu Leu Gln Val Glu Gly Leu Ser Asp
165 170 175

CTC AGG CTG GAA CTT CAC AGC AAG AAG ATG AAC CTG CAC TTG GTT CTC 576
Leu Arg Leu Glu Leu His Ser Lys Lys Met Asn Leu His Leu Val Leu

180 185 190

ATA GAG GAA CTG CAC CGA CAT CTG TAC ATC AAA TCC ACT AGC CGG GTT 624
Ile Glu Glu Leu His Arg His Leu Tyr Ile Lys Ser Thr Ser Arg Val
195 200 205

GTA CAG CGT AAC AAG GAA AAA GGG AAG ATG AGT TCT CAT GGC AAA GAT 672
Val Gln Arg Asn Lys Glu Lys Gly Lys Met Ser Ser His Gly Lys Asp
210 215 220

GCT TCT CCT GGT CCT CTG ATT GAT GTT TCA AAC ATC TCT ACT CCA CGC 720
Ala Ser Pro Gly Pro Leu Ile Asp Val Ser Asn Ile Ser Thr Pro Arg
225 230 235 240

AAA TTC CTT GAT GCC ACT CAA TAT TCT GCT GCT GGA AGC TCA AGT GTG 768
Lys Phe Leu Asp Ala Thr Gln Tyr Ser Ala Ala Gly Ser Ser Ser Val
245 250 255

AGG GAG ATG AAC CTG CAG GAC ATC AAA GAG GAC TTG GAC TGT GAT CCT 816
Arg Glu Met Asn Leu Gln Asp Ile Lys Glu Asp Leu Asp Cys Asp Pro
260 265 270

GAG GAG AAC AGC ACT CTT TTC ATG GGA ATT CTT ATT CAG GGG CTG GCC 864
Glu Glu Asn Ser Thr Leu Phe Met Gly Ile Leu Ile Gln Gly Leu Ala
275 280 285

AGA CTG AAG AAG ATC CCT GAG ACC GTT AAA GCC ATT AAA GAG CGT TTG 912
Arg Leu Lys Lys Ile Pro Glu Thr Val Lys Ala Ile Lys Glu Arg Leu
290 295 300

GAG CAG GAG CTA AAG CAG ATT GTG AAG AGG TCA ACC ACC CAG GTG GCA 960
Glu Gln Glu Leu Lys Gln Ile Val Lys Arg Ser Thr Thr Gln Val Ala
305 310 315 320

GAC AGT GCC TAT CAG AGG GGA GAG AGC CTC ACT GTG GAC AAC CAG CCA 1008
Asp Ser Ala Tyr Gln Arg Gly Glu Ser Leu Thr Val Asp Asn Gln Pro
325 330 335

AGG TTA CTT CTA GAA CTG CTG GAA CTG TTG TTT GAT AAG TTT AAT GCT 1056
Arg Leu Leu Leu Glu Leu Leu Glu Leu Leu Phe Asp Lys Phe Asn Ala
340 345 350

GTA GCC AGT GCA CAT TCT ATA GTC CTG GGG TAC CTT CAG GAC TCT GTG 1104

```
Val Ala Ser Ala His Ser Ile Val Leu Gly Tyr Leu Gln Asp Ser Val
        355                 360                 365

GGG ACC CAG CCA ACA CAG CAG GAA GAG ATC AAA TTA TAC GAT ATG GCA      1152
Gly Thr Gln Pro Thr Gln Gln Glu Glu Ile Lys Leu Tyr Asp Met Ala
    370                 375                 380

GAT GTG TGG GTG AAG ATC CAG GAT GTG CTG CAG ATG CTG TTG ACT GAA      1200
Asp Val Trp Val Lys Ile Gln Asp Val Leu Gln Met Leu Leu Thr Glu
385                 390                 395                 400

TAC TTG GAT ATG AAG AAC ACA CGT ACT GCG TCA GAG CCG TCA GCT CAA      1248
Tyr Leu Asp Met Lys Asn Thr Arg Thr Ala Ser Glu Pro Ser Ala Gln
                405                 410                 415

CTA AGC TAT GCC AGT ACT GGA CGA GAG TTC GCA GCC TTT TTT GCC AAG      1296
Leu Ser Tyr Ala Ser Thr Gly Arg Glu Phe Ala Ala Phe Phe Ala Lys
            420                 425                 430

AAG AAA CCA CAA AGG CCA AAG AAT TCT CTT TTC AAG TTT GAA TCA TCC      1344
Lys Lys Pro Gln Arg Pro Lys Asn Ser Leu Phe Lys Phe Glu Ser Ser
        435                 440                 445

TCC CAT GCT ATC AGT ATG AGC GCC TAT CTC CGA GAA CAG AGA AGG GAG      1392
Ser His Ala Ile Ser Met Ser Ala Tyr Leu Arg Glu Gln Arg Arg Glu
    450                 455                 460

CTG TAC AGT CGG AGT GGA GAA CTT CAA GGA GGT CCT GAT GAC AAC TTA      1440
Leu Tyr Ser Arg Ser Gly Glu Leu Gln Gly Gly Pro Asp Asp Asn Leu
465                 470                 475                 480

ATT GAA GGT GGA GGA ACA AAA TTT GTC TGC AAA CCT GGA GCC AGA AAT      1488
Ile Glu Gly Gly Gly Thr Lys Phe Val Cys Lys Pro Gly Ala Arg Asn
                485                 490                 495

ATT ACC GTC ATA TTC CAT CCA CTG CTG AGA TTT ATT CAG GAG ATT GAG      1536
Ile Thr Val Ile Phe His Pro Leu Leu Arg Phe Ile Gln Glu Ile Glu
            500                 505                 510

CAT GCC CTG GGA CTT GGC CCT GCC AAA CAG TGT CTC CTT CGA GAG TTT      1584
His Ala Leu Gly Leu Gly Pro Ala Lys Gln Cys Leu Leu Arg Glu Phe
        515                 520                 525

CTC ACT ATA TAT ATC AAG AAC ATC TTC CTT AAT CAG GTC TTG ACT GAG      1632
```

Leu Thr Ile Tyr Ile Lys Asn Ile Phe Leu Asn Gln Val Leu Thr Glu
530 535 540

ATC AAC AAG GAG ATC GAA GGT GTC ACC AAA ACC TCA GAC CCC TTG AAG 1680
Ile Asn Lys Glu Ile Glu Gly Val Thr Lys Thr Ser Asp Pro Leu Lys
545 550 555 560

ATC CTA GCT AAT GCA GAC ACC ATG AAG GTT CTG GGC GTG CAG AGG CCT 1728
Ile Leu Ala Asn Ala Asp Thr Met Lys Val Leu Gly Val Gln Arg Pro
565 570 575

CTT CTA CAG AGC ACC ATC ATC GTG GAG AAG ACA GTA CAA GAC CTC ATG 1776
Leu Leu Gln Ser Thr Ile Ile Val Glu Lys Thr Val Gln Asp Leu Met
580 585 590

AAC CTG ATG CAT GAC TTG AGT GCA TAT TCA GAT CAG TTC CTC AAC ATG 1824
Asn Leu Met His Asp Leu Ser Ala Tyr Ser Asp Gln Phe Leu Asn Met
595 600 605

GTG TGT GTG AAG CTA CAG GAA TAC AAG GAC ACA TGC TCC ACA GCC TAC 1872
Val Cys Val Lys Leu Gln Glu Tyr Lys Asp Thr Cys Ser Thr Ala Tyr
610 615 620

AGA GGC ATT GTC CAA TCA GAA GAG AAA CTT GTC ATC AGT GCA TCT TGG 1920
Arg Gly Ile Val Gln Ser Glu Glu Lys Leu Val Ile Ser Ala Ser Trp
625 630 635 640

GCA AAA GAT GAT GAT ATC AGC AGA CTC TTG AAA TCA CTG CCG AAC TGG 1968
Ala Lys Asp Asp Asp Ile Ser Arg Leu Leu Lys Ser Leu Pro Asn Trp
645 650 655

ACT AAC ATG GCT CAG CCC AAA CAG CTA AGG CCT AAG AGA GAG GAG GAG 2016
Thr Asn Met Ala Gln Pro Lys Gln Leu Arg Pro Lys Arg Glu Glu Glu
660 665 670

GAA GAC TTC ATA AGG GCA GCC TTT GGC AAG GAG TCT GAG GTT CTG ATT 2064
Glu Asp Phe Ile Arg Ala Ala Phe Gly Lys Glu Ser Glu Val Leu Ile
675 680 685

GGA AAC CTT GGT GAC AAA CTC ATT CCT CCA CAA GAT ATT CTC CGT GAC 2112
Gly Asn Leu Gly Asp Lys Leu Ile Pro Pro Gln Asp Ile Leu Arg Asp
690 695 700

GTC AGT GAC CTC AAA GCC TTG GCC AAC ATG CAT GAA AGC CTG GAA TGG 2160

Val Ser Asp Leu Lys Ala Leu Ala Asn Met His Glu Ser Leu Glu Trp
705 710 715 720

CTG GCA GGC CGA ACA AAG TCA GCT TTC TCC AGC CTT TCT GCA TCC CAG 2208
Leu Ala Gly Arg Thr Lys Ser Ala Phe Ser Ser Leu Ser Ala Ser Gln
725 730 735

ATG CTT TCC CCT GCT CAA GAG AGC CAC GTA AAC ATG GAC CTT CCT CCA 2256
Met Leu Ser Pro Ala Gln Glu Ser His Val Asn Met Asp Leu Pro Pro
740 745 750

GTG TCT GAA CAG ATC ATG CAG ACG CTG AGT GAA CTT GCC AAG TCC TTC 2304
Val Ser Glu Gln Ile Met Gln Thr Leu Ser Glu Leu Ala Lys Ser Phe
755 760 765

CAG GAC ATG GCT GAC CGC TGC TTG CTC GTC TTG CAT CTG GAA GTG AGA 2352
Gln Asp Met Ala Asp Arg Cys Leu Leu Val Leu His Leu Glu Val Arg
770 775 780

GTT CAT TGT TTC CAC TAT CTC ATC CCT CTG GCA AAG GAG GGG AAC TAT 2400
Val His Cys Phe His Tyr Leu Ile Pro Leu Ala Lys Glu Gly Asn Tyr
785 790 795 800

GCC ATT GTG GCC AAT GTG GAA AGC ATG GAT TAT GAC CCT TTA GTG GTC 2448
Ala Ile Val Ala Asn Val Glu Ser Met Asp Tyr Asp Pro Leu Val Val
805 810 815

AAG CTC AAC AAA GAC ATC AGT GCC ATG GAA GAG GCC ATG AGC GCC AGC 2496
Lys Leu Asn Lys Asp Ile Ser Ala Met Glu Glu Ala Met Ser Ala Ser
820 825 830

CTC CAG CAA CAC AAG TTC CAG TAC ATC TTC GAA GGT CTG GGA CAC CTC 2544
Leu Gln Gln His Lys Phe Gln Tyr Ile Phe Glu Gly Leu Gly His Leu
835 840 845

ATC TCC TGT ATC CTC ATT AAT GGG GCT CAG TAC TTC CGG CGC ATC AGT 2592
Ile Ser Cys Ile Leu Ile Asn Gly Ala Gln Tyr Phe Arg Arg Ile Ser
850 855 860

GAG TCT GGC ATC AAG AAA ATG TGT AGA AAC ATT TTT GTT CTT CAG CAG 2640
Glu Ser Gly Ile Lys Lys Met Cys Arg Asn Ile Phe Val Leu Gln Gln
865 870 875 880

AAT TTG ACC AAC ATC ACC ATG TCA CGG GAG GCA GAC TTG GAC TTT GCA 2688

Asn Leu Thr Asn Ile Thr Met Ser Arg Glu Ala Asp Leu Asp Phe Ala
885 890 895

AGA CAG TAC TAC GAG ATG CTG TAC AAC ACT GCT GAT GAG CTC CTG AAC 2736
Arg Gln Tyr Tyr Glu Met Leu Tyr Asn Thr Ala Asp Glu Leu Leu Asn
900 905 910

CTG GTG GTG GAC CAG GGT GTG AAA TAC ACA GAG CTA GAG TAC ATC CAT 2784
Leu Val Val Asp Gln Gly Val Lys Tyr Thr Glu Leu Glu Tyr Ile His
915 920 925

GCC CTG ACC CTG CTG CAC CGA AGC CAG ACT GGC GTG GGG GAC CAG ACC 2832
Ala Leu Thr Leu Leu His Arg Ser Gln Thr Gly Val Gly Asp Gln Thr
930 935 940

ACC CAG AAC ACC AGG CTG CAG AGA CTC AAG GAG ATC ATC TGT GAG CAG 2880
Thr Gln Asn Thr Arg Leu Gln Arg Leu Lys Glu Ile Ile Cys Glu Gln
945 950 955 960

GCT GCC ATC AAG CAA GCC ACC AAG GAC AAG AAA ATA ACC ACT GTG 2925
Ala Ala Ile Lys Gln Ala Thr Lys Asp Lys Lys Ile Thr Thr Val
965 970 975

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 975 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Met Ala Ala Glu Ala Ala Gly Gly Lys Tyr Arg Ser Thr Val Ser Lys
1 5 10 15

Ser Lys Asp Pro Ser Gly Leu Leu Ile Ser Val Ile Arg Thr Leu Ser
20 25 30

Thr Ser Asp Asp Val Glu Asp Arg Glu Asn Glu Lys Gly Arg Leu Glu
35 40 45

Glu Ala Tyr Glu Lys Cys Asp Arg Asp Leu Asp Glu Leu Ile Val Gln

50 55 60

His Tyr Thr Glu Leu Thr Thr Ala Ile Arg Thr Tyr Gln Ser Ile Thr
65 70 75 80

Glu Arg Ile Thr Asn Ser Arg Asn Lys Ile Lys Gln Val Lys Glu Asn
85 90 95

Leu Leu Ser Cys Lys Met Leu Leu His Cys Lys Arg Asp Glu Leu Arg
100 105 110

Lys Leu Trp Ile Glu Gly Ile Glu His Lys His Val Leu Asn Leu Leu
115 120 125

Asp Glu Ile Glu Asn Ile Lys Gln Val Pro Gln Lys Leu Glu Gln Cys
130 135 140

Met Ala Ser Lys His Tyr Leu Ser Ala Thr Asp Met Leu Val Ser Ala
145 150 155 160

Val Glu Ser Leu Glu Gly Pro Leu Leu Gln Val Glu Gly Leu Ser Asp
165 170 175

Leu Arg Leu Glu Leu His Ser Lys Lys Met Asn Leu His Leu Val Leu
180 185 190

Ile Glu Glu Leu His Arg His Leu Tyr Ile Lys Ser Thr Ser Arg Val
195 200 205

Val Gln Arg Asn Lys Glu Lys Gly Lys Met Ser Ser His Gly Lys Asp
210 215 220

Ala Ser Pro Gly Pro Leu Ile Asp Val Ser Asn Ile Ser Thr Pro Arg
225 230 235 240

Lys Phe Leu Asp Ala Thr Gln Tyr Ser Ala Ala Gly Ser Ser Ser Val
245 250 255

Arg Glu Met Asn Leu Gln Asp Ile Lys Glu Asp Leu Asp Cys Asp Pro
260 265 270

Glu Glu Asn Ser Thr Leu Phe Met Gly Ile Leu Ile Gln Gly Leu Ala
275 280 285

Arg Leu Lys Lys Ile Pro Glu Thr Val Lys Ala Ile Lys Glu Arg Leu
290 295 300

Glu Gln Glu Leu Lys Gln Ile Val Lys Arg Ser Thr Thr Gln Val Ala
305 310 315 320

Asp Ser Ala Tyr Gln Arg Gly Glu Ser Leu Thr Val Asp Asn Gln Pro
325 330 335

Arg Leu Leu Leu Glu Leu Leu Glu Leu Leu Phe Asp Lys Phe Asn Ala
340 345 350

Val Ala Ser Ala His Ser Ile Val Leu Gly Tyr Leu Gln Asp Ser Val
355 360 365

Gly Thr Gln Pro Thr Gln Gln Glu Glu Ile Lys Leu Tyr Asp Met Ala
370 375 380

Asp Val Trp Val Lys Ile Gln Asp Val Leu Gln Met Leu Leu Thr Glu
385 390 395 400

Tyr Leu Asp Met Lys Asn Thr Arg Thr Ala Ser Glu Pro Ser Ala Gln
405 410 415

Leu Ser Tyr Ala Ser Thr Gly Arg Glu Phe Ala Ala Phe Phe Ala Lys
420 425 430

Lys Lys Pro Gln Arg Pro Lys Asn Ser Leu Phe Lys Phe Glu Ser Ser
435 440 445

Ser His Ala Ile Ser Met Ser Ala Tyr Leu Arg Glu Gln Arg Arg Glu
450 455 460

Leu Tyr Ser Arg Ser Gly Glu Leu Gln Gly Gly Pro Asp Asp Asn Leu
465 470 475 480

Ile Glu Gly Gly Gly Thr Lys Phe Val Cys Lys Pro Gly Ala Arg Asn
485 490 495

Ile Thr Val Ile Phe His Pro Leu Leu Arg Phe Ile Gln Glu Ile Glu
500 505 510

His Ala Leu Gly Leu Gly Pro Ala Lys Gln Cys Leu Leu Arg Glu Phe
515 520 525

Leu Thr Ile Tyr Ile Lys Asn Ile Phe Leu Asn Gln Val Leu Thr Glu
530 535 540

Ile Asn Lys Glu Ile Glu Gly Val Thr Lys Thr Ser Asp Pro Leu Lys
545 550 555 560

Ile Leu Ala Asn Ala Asp Thr Met Lys Val Leu Gly Val Gln Arg Pro
565 570 575

Leu Leu Gln Ser Thr Ile Ile Val Glu Lys Thr Val Gln Asp Leu Met
580 585 590

Asn Leu Met His Asp Leu Ser Ala Tyr Ser Asp Gln Phe Leu Asn Met
595 600 605

Val Cys Val Lys Leu Gln Glu Tyr Lys Asp Thr Cys Ser Thr Ala Tyr
610 615 620

Arg Gly Ile Val Gln Ser Glu Glu Lys Leu Val Ile Ser Ala Ser Trp
625 630 635 640

Ala Lys Asp Asp Asp Ile Ser Arg Leu Leu Lys Scr Leu Pro Asn Trp
645 650 655

Thr Asn Met Ala Gln Pro Lys Gln Leu Arg Pro Lys Arg Glu Glu Glu
660 665 670

Glu Asp Phe Ile Arg Ala Ala Phe Gly Lys Glu Ser Glu Val Leu Ile
675 680 685

Gly Asn Leu Gly Asp Lys Leu Ile Pro Pro Gln Asp Ile Leu Arg Asp
690 695 700

Val Ser Asp Leu Lys Ala Leu Ala Asn Met His Glu Ser Leu Glu Trp
705 710 715 720

Leu Ala Gly Arg Thr Lys Ser Ala Phe Ser Ser Leu Ser Ala Ser Gln
725 730 735

Met Leu Ser Pro Ala Gln Glu Ser His Val Asn Met Asp Leu Pro Pro
740 745 750

Val Ser Glu Gln Ile Met Gln Thr Leu Ser Glu Leu Ala Lys Ser Phe
755 760 765

Gln Asp Met Ala Asp Arg Cys Leu Leu Val Leu His Leu Glu Val Arg
770 775 780

Val His Cys Phe His Tyr Leu Ile Pro Leu Ala Lys Glu Gly Asn Tyr
785 790 795 800

Ala Ile Val Ala Asn Val Glu Ser Met Asp Tyr Asp Pro Leu Val Val
805 810 815

Lys Leu Asn Lys Asp Ile Ser Ala Met Glu Glu Ala Met Ser Ala Ser
820 825 830

Leu Gln Gln His Lys Phe Gln Tyr Ile Phe Glu Gly Leu Gly His Leu
835 840 845

Ile Ser Cys Ile Leu Ile Asn Gly Ala Gln Tyr Phe Arg Arg Ile Ser
850 855 860

Glu Ser Gly Ile Lys Lys Met Cys Arg Asn Ile Phe Val Leu Gln Gln
865 870 875 880

Asn Leu Thr Asn Ile Thr Met Ser Arg Glu Ala Asp Leu Asp Phe Ala
885 890 895

Arg Gln Tyr Tyr Glu Met Leu Tyr Asn Thr Ala Asp Glu Leu Leu Asn
900 905 910

Leu Val Val Asp Gln Gly Val Lys Tyr Thr Glu Leu Glu Tyr Ile His
915 920 925

Ala Leu Thr Leu Leu His Arg Ser Gln Thr Gly Val Gly Asp Gln Thr
930 935 940

Thr Gln Asn Thr Arg Leu Gln Arg Leu Lys Glu Ile Ile Cys Glu Gln
945 950 955 960

Ala Ala Ile Lys Gln Ala Thr Lys Asp Lys Lys Ile Thr Thr Val
965 970 975

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid

(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: rsec6.3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

Ala Ala Ile Gln Ser Gln Leu Asp Gly Val Arg Thr Gly Leu Ser Gln
1 5 10 15

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 13 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: rsec8.1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Xaa Ala Pro Glu Gly Pro Leu Ile Asp Val Xaa Asn Ile
1 5 10

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: rsec8.2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

Glu Phe Ala Ala Phe Phe Ala Lys
1 5

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: rsec8.3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Xaa Leu Gly Val Gln Arg Pro Leu Leu Gln Ser Thr Ser Ile Xaa Glu
1 5 10 15

(2) INFORMATION FOR SEQ ID NO:11:

60

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p71.3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

Leu His Leu Ile Ala Gln Glu Leu Pro Phe Asp Arg Phe Ser Glu Val
1 5 10 15

Lys

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79.1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Xaa Thr Asp Tyr Ile Ala Glu
1 5

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79.2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Glu Thr Tyr Gly Ala Phe Leu Ser Arg Ser Xaa Gly
1 5 10

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79.3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Xaa Xaa Pro Pro Gln Gly Val Pro Tyr Asn Pro Ala Ser Pro
1 5 10

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79.4

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

Xaa Xaa Gln Glu Glu Glu Thr Leu Met Phe Ile Arg Gly Asn
1 5 10

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79.5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Ala Leu Phe Ile Arg Asp Asp Xaa Gln Phe
1 5 10

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79.6

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

Asn Leu Pro Val Phe Gln Ser Cys Leu
1 5

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79.7

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Ala Val Glu Tyr Phe Gln Asp Lys Phe Pro Asp
1 5 10

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79.8

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

Tyr Arg Val Glu Gln Val Gly Asp Met Ile Asp Arg Leu Phe Asp Thr
1 5 10 15
Ser

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79.9

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Val Tyr Glu Asp Pro Ala Leu Ser Ala Ile Phe Leu His Asn Asn Tyr
1 5 10 15

Asn Tyr

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79.10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Xaa Xaa Tyr Gly Ala Phe Leu His Arg Tyr Ser Ser Val Pro Phe Val
1 5 10 15

Tyr Gly Xaa His
20

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p84.1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Gln Leu Ser Gln Gln Ser Asp Gly Asp Arg Asp Leu Gln Glu Trp Arg
1 5 10 15

Gln Arg Val Gln Ala Leu Ala Glu Glu Thr Ala Gln Tyr Lys
20 25 30

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p84.2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Xaa Leu Gln Leu Ser Phe Asn Phe Ser Glu Pro Asn Arg Gln Arg Pro
1 5 10 15

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p84.3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Ser Ile Pro Leu Ala Leu Leu Pro Ala Ala Ala Ala Gly Ala
1 5 10

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p84.4

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

Asp Ala Val Xaa Gln Asn Ser Thr Gln Ala Ala Glu Thr Glu Asn
1 5 10 15

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p84.5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Asp Tyr Arg Asn Asp Glu Ala
1 5

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p84.6

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

Glu Asn Asn Pro Glu Glu Asp Asp Pro Ser
1 5 10

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p84.7

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

Xaa Leu Ser Gln Gln Ser Asp Xaa Gly
1 5

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p84.8

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

Ala Ala Ala Leu Arg Ala Pro Pro Xaa Val Thr Ser
1 5 10

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p84.9

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

Xaa Lys Arg Glu Pro Leu Glu
1 5

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p96.1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

Val Val Gly Gln Phe Pro Phe Gln Asp Thr Glu Leu Glu Lys
1 5 10

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p96.2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Xaa Val Tyr Glu Ile Phe Asp Asn
1 5

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p96.3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:
Asp Phe Leu Glu Ser Ile Arg
1 5

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 14 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p96.4

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Xaa Asp Gln Asp Leu Gln Leu Ala Asp Tyr Asp His Met Thr
1 5 10

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p96.5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Ser Thr Asn Leu Leu Leu Thr Arg Thr Leu Xaa Asn
1 5 10

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p102.1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

Tyr Leu Ser Gly Leu Gln Ala Pro Gly Xaa Pro Ala Ser Gln Ser Ile
1 5 10 15

Gly Ala Gln

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p102.2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

Gly Gly Leu Ser Thr Phe Phe Glu Ala Gln Asp Ala Leu Ser Ala Ile
1 5 10 15

His Gln Lys

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids

(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p102.3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

Ala Ser Asn Thr Ala Asp Thr Xaa Arg Gln Glu Arg
1 5 10

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p102.4

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

Xaa Arg Glu Asn Tyr Ile Glu Gly Gly Ile
1 5 10

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p102.5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

Glu Asn Leu Gly Arg Leu Phe Glu Asn Tyr Ile
1 5 10

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p102.6

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

Xaa Asp Tyr Asp Val Val Ile Asn Asp Tyr Glu
1 5 10

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p102.7

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

Xaa Ile Pro Xaa Leu Ser Thr Arg Pro Ala Asn Pro
1 5 10

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p106.1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

Xaa Xaa Tyr Gly Glu Ile Ala Xaa Lys
1 5

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p106.2

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

Xaa Ala Thr Val Ser Leu Pro Glu Lys
1 5

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p106.3

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

Xaa Asp Tyr Gly Val Ile Ala Asn Asp
1 5

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p106.4

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

Leu Ile Lys Tyr Phe Phe Met Val Ala Ser Val Lys
1 5 10

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p106.5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

Glu Leu Pro Glu Phe Asn Leu His Phe Phe Lys
1 5 10

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p106.6

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

Xaa Leu Gln Asp Val Asp Leu Ala Ser Xaa Arg
1 5 10

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p106.7

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:
Xaa Asn Arg Xaa Asn Glu Pro Ala Val Asn Val Leu
1 5 10

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 13 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p106.8

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

Xaa Gln Leu Xaa Asn Ile Val Glu Pro Glu Xaa Ile Tyr
1 5 10

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2127 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p71 (rsec10)

(ix) FEATURE:
(A) NAME/KEY: Coding Sequence
(B) LOCATION: 1...2124

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

```
ATG GCC ACG ACG GCC GAG CTC TTC GAG GAG CCT TTT GTG GCC GAT GAA      48
Met Ala Thr Thr Ala Glu Leu Phe Glu Glu Pro Phe Val Ala Asp Glu
 1               5                  10                  15

TAC ATT GAA CGT CTC GTG TGG AGA ACC CCG GGA GGT GGT TCT AGG GGT      96
Tyr Ile Glu Arg Leu Val Trp Arg Thr Pro Gly Gly Gly Ser Arg Gly
            20                  25                  30

GGA CCT GAA GCT TTT GAT CCT AAA AGG TTA TTA GAA GAA TTT GTG AAT     144
Gly Pro Glu Ala Phe Asp Pro Lys Arg Leu Leu Glu Glu Phe Val Asn
        35                  40                  45

CAT ATT CAA GAA CTA CAG ATA ATG GAT GAA AGG ATT CAA AGG AAA GTA     192
His Ile Gln Glu Leu Gln Ile Met Asp Glu Arg Ile Gln Arg Lys Val
    50                  55                  60

GAG AAG TTA GAA CAG CAG TGT CAG AAG GAG GCA AAG GAG TTT GCT AAG     240
Glu Lys Leu Glu Gln Gln Cys Gln Lys Glu Ala Lys Glu Phe Ala Lys
65                  70                  75                  80

AAG GTA CAA GAG CTG CAG AAA AGC AAC CAG GTT GCT TTC CAA CAT TTC     288
Lys Val Gln Glu Leu Gln Lys Ser Asn Gln Val Ala Phe Gln His Phe
                85                  90                  95

CAA GAA CTA GAT GAA CAC ATT AGC TAT GTA GCT ACC AAA GTG TGT CAC     336
Gln Glu Leu Asp Glu His Ile Ser Tyr Val Ala Thr Lys Val Cys His
            100                 105                 110

CTT GGA GAC CAG TTG GAA GGG GTA AAC ACA CCT AGA CAG CGT GCA GTG     384
Leu Gly Asp Gln Leu Glu Gly Val Asn Thr Pro Arg Gln Arg Ala Val
        115                 120                 125

GAG GCG CAG AAA TTG ATG AAA TAC TTT AAT GAG TTT CTA GAT GGA GAA     432
Glu Ala Gln Lys Leu Met Lys Tyr Phe Asn Glu Phe Leu Asp Gly Glu
    130                 135                 140

TTG AAA TCT GAT GTT TTT ACA AAT CCT GAA AAG ATC AAG GAA GCA GCA     480
Leu Lys Ser Asp Val Phe Thr Asn Pro Glu Lys Ile Lys Glu Ala Ala
145                 150                 155                 160

GAC GTC ATT CAG AAA CTG CAT CTG ATC GCC CAG GAG TTA CCT TTC GAT     528
Asp Val Ile Gln Lys Leu His Leu Ile Ala Gln Glu Leu Pro Phe Asp
                165                 170                 175

AGG TTT TCA GAA GTA AAA TCC AAA ATT GCA AGT AAA TAC CAC GAC TTA     576
```

```
Arg Phe Ser Glu Val Lys Ser Lys Ile Ala Ser Lys Tyr His Asp Leu
            180                 185                 190

GAA TGC CAG CTG ATT CAG GAG TTT ACC AGT GCA CAA CGA AGA GGT GAG     624
Glu Cys Gln Leu Ile Gln Glu Phe Thr Ser Ala Gln Arg Arg Gly Glu
        195                 200                 205

GTC TCC CGG ATG AGG GAG GTG GCA GCT GTC CTG CTT CAT TTT AAG GGT     672
Val Ser Arg Met Arg Glu Val Ala Ala Val Leu Leu His Phe Lys Gly
    210                 215                 220

TAT TCC CAC TGT ATT GAT GTT TAT ATA AAG CAG TGC CAG GAG GGT GCT     720
Tyr Ser His Cys Ile Asp Val Tyr Ile Lys Gln Cys Gln Glu Gly Ala
225                 230                 235                 240

TAC TTG AGA AAT GAT ATA TTC GAA GAC GCA GCA ATT CTC TGT CAG CGA     768
Tyr Leu Arg Asn Asp Ile Phe Glu Asp Ala Ala Ile Leu Cys Gln Arg
                245                 250                 255

GTG AAC AAG CAA GTT GGA GAT ATC TTT AGT AAT CCA GAA GCA GTA CTG     816
Val Asn Lys Gln Val Gly Asp Ile Phe Ser Asn Pro Glu Ala Val Leu
            260                 265                 270

GCT AAG CTT ATT CAG AAT GTG TTT GAA GTC AAA CTA CAG AGT TTT GTG     864
Ala Lys Leu Ile Gln Asn Val Phe Glu Val Lys Leu Gln Ser Phe Val
        275                 280                 285

AAA GAT CAG TTA GAA GAA TGT AGG AAA TCG GAT GCT GAG CAG TAT CTT     912
Lys Asp Gln Leu Glu Glu Cys Arg Lys Ser Asp Ala Glu Gln Tyr Leu
    290                 295                 300

AAA AGT CTG TAT GAT CTG TAC ACA AGA ACC ACC AGT CTT TCC AGC AAA     960
Lys Ser Leu Tyr Asp Leu Tyr Thr Arg Thr Thr Ser Leu Ser Ser Lys
305                 310                 315                 320

TTG ATG GAG TTT AAC TTA GGT ACT GAT AAA CAG ACT TTC TTG TCT AAG    1008
Leu Met Glu Phe Asn Leu Gly Thr Asp Lys Gln Thr Phe Leu Ser Lys
                325                 330                 335

CTT ATC AAA TCC ATT TTC GTT TCC TAT CTG GAG AAC TAT ATT GAA GTG    1056
Leu Ile Lys Ser Ile Phe Val Ser Tyr Leu Glu Asn Tyr Ile Glu Val
            340                 345                 350

GAG ATT GGA TAT TTG AAA AGC AGA AGT GCT ATG ATC CTA CAG CGC TAT    1104
```

Glu Ile Gly Tyr Leu Lys Ser Arg Ser Ala Met Ile Leu Gln Arg Tyr
355 360 365

TAT GAT TCA AAA AAC CAC CAA AAG AGA TCC ATT GGC ACA GGA GGT ATT 1152
Tyr Asp Ser Lys Asn His Gln Lys Arg Ser Ile Gly Thr Gly Gly Ile
370 375 380

CAA GAT TTG AAA GAA AGG ATT AGA CAA CGT ACC AAC TTA CCA CTG GGG 1200
Gln Asp Leu Lys Glu Arg Ile Arg Gln Arg Thr Asn Leu Pro Leu Gly
385 390 395 400

CCA AGT ATT GAC ACA CAT GGG GAG ACT TTC CTA TCT CAA GAA GTG GTA 1248
Pro Ser Ile Asp Thr His Gly Glu Thr Phe Leu Ser Gln Glu Val Val
405 410 415

GTT AAT CTT TTA CAA GAA ACC AAA CAA GCC TTT GAA AGA TGT CAT AGG 1296
Val Asn Leu Leu Gln Glu Thr Lys Gln Ala Phe Glu Arg Cys His Arg
420 425 430

CTT TCT GAT CCT TCT GAT TTA CCA AGG AAT GCC TTT AGA ATT TTT ACC 1344
Leu Ser Asp Pro Ser Asp Leu Pro Arg Asn Ala Phe Arg Ile Phe Thr
435 440 445

ATT CTT GTG GAA TTT TTA TGT ATT GAG CAT ATT GAT TAT GCT TTA GAA 1392
Ile Leu Val Glu Phe Leu Cys Ile Glu His Ile Asp Tyr Ala Leu Glu
450 455 460

ACG GGG CTT GCT GGA ATT CCA TCA TCA GAT TCT AGG AAC GCA AAT CTC 1440
Thr Gly Leu Ala Gly Ile Pro Ser Ser Asp Ser Arg Asn Ala Asn Leu
465 470 475 480

TAT TTT TTG GAT GTT GTA CAA CAG GCC AAT ACT ATT TTT CAT CTT TTT 1488
Tyr Phe Leu Asp Val Val Gln Gln Ala Asn Thr Ile Phe His Leu Phe
485 490 495

GAC AAA CAG TTT AAT GAT CAC CTA ATG CCA CTA ATA AGC TCT TCT CCT 1536
Asp Lys Gln Phe Asn Asp His Leu Met Pro Leu Ile Ser Ser Ser Pro
500 505 510

AAG TTG TCT GAA TGC CTC CAG AAG AAG AAG GAG ATA ATT GAG CAG ATG 1584
Lys Leu Ser Glu Cys Leu Gln Lys Lys Lys Glu Ile Ile Glu Gln Met
515 520 525

GAG ATG AAG TTG GAC ACT GGC ATC GAT AGG ACG TTA AAT TGT ATG ATT 1632

Glu Met Lys Leu Asp Thr Gly Ile Asp Arg Thr Leu Asn Cys Met Ile
530 535 540

GGA CAG ATG AAG CAC ATC TTG GCT GCA GAA CAA AAG AAA ACA GAT TTT 1680
Gly Gln Met Lys His Ile Leu Ala Ala Glu Gln Lys Lys Thr Asp Phe
545 550 555 560

AAG CCA GAA GAT GAA AAC AAT GTT TTG ATT CAG TAT ACT AAT GCA TGT 1728
Lys Pro Glu Asp Glu Asn Asn Val Leu Ile Gln Tyr Thr Asn Ala Cys
565 570 575

GTA AAG GTT TGT GCT TAT GTA AGA AAA CAA GTT GAG AAG ATT AAG AAT 1776
Val Lys Val Cys Ala Tyr Val Arg Lys Gln Val Glu Lys Ile Lys Asn
580 585 590

TCC ATG GAT GGG AAG AAT GTG GAC ACG GTT CTG ATG GAG CTC GGA GTA 1824
Ser Met Asp Gly Lys Asn Val Asp Thr Val Leu Met Glu Leu Gly Val
595 600 605

CGT TTC CAC CGG CTT ACT TAT GAG CAT CTT CAA CAA TAT TCC TAC AGT 1872
Arg Phe His Arg Leu Thr Tyr Glu His Leu Gln Gln Tyr Ser Tyr Ser
610 615 620

TGT ATG GGC GGC ATG CTT GCA ATT TGC GAC GTT GCT GAA TAT AGA AAA 1920
Cys Met Gly Gly Met Leu Ala Ile Cys Asp Val Ala Glu Tyr Arg Lys
625 630 635 640

TGT GCC AAA GAC TTC AAG ATT CCA ATG GTA TTA CAT CTT TTT GAT ACT 1968
Cys Ala Lys Asp Phe Lys Ile Pro Met Val Leu His Leu Phe Asp Thr
645 650 655

CTG CAT GCA CTT TGC AAT CTC CTA GTC GTT GCT CCA GAT AAT TTA AAG 2016
Leu His Ala Leu Cys Asn Leu Leu Val Val Ala Pro Asp Asn Leu Lys
660 665 670

CAA GTC TGC TCA GGA GAA CAA CTG GCC AAT CTG GAC AAG AAC ATA CTC 2064
Gln Val Cys Ser Gly Glu Gln Leu Ala Asn Leu Asp Lys Asn Ile Leu
675 680 685

CAC TCC TTC GTC CAG CTT CGA GCT GAC TAT AGA TCC GCC CGC CTG GCT 2112
His Ser Phe Val Gln Leu Arg Ala Asp Tyr Arg Ser Ala Arg Leu Ala
690 695 700

CGG CAC TTC AGC TGA 2127

Arg His Phe Ser
705

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 708 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

Met Ala Thr Thr Ala Glu Leu Phe Glu Glu Pro Phe Val Ala Asp Glu
1 5 10 15

Tyr Ile Glu Arg Leu Val Trp Arg Thr Pro Gly Gly Gly Ser Arg Gly
20 25 30
Gly Pro Glu Ala Phe Asp Pro Lys Arg Leu Leu Glu Glu Phe Val Asn
35 40 45
His Ile Gln Glu Leu Gln Ile Met Asp Glu Arg Ile Gln Arg Lys Val
50 55 60
Glu Lys Leu Glu Gln Gln Cys Gln Lys Glu Ala Lys Glu Phe Ala Lys
65 70 75 80
Lys Val Gln Glu Leu Gln Lys Ser Asn Gln Val Ala Phe Gln His Phe
85 90 95
Gln Glu Leu Asp Glu His Ile Ser Tyr Val Ala Thr Lys Val Cys His
100 105 110
Leu Gly Asp Gln Leu Glu Gly Val Asn Thr Pro Arg Gln Arg Ala Val
115 120 125
Glu Ala Gln Lys Leu Met Lys Tyr Phe Asn Glu Phe Leu Asp Gly Glu
130 135 140
Leu Lys Ser Asp Val Phe Thr Asn Pro Glu Lys Ile Lys Glu Ala Ala
145 150 155 160
Asp Val Ile Gln Lys Leu His Leu Ile Ala Gln Glu Leu Pro Phe Asp
165 170 175
Arg Phe Ser Glu Val Lys Ser Lys Ile Ala Ser Lys Tyr His Asp Leu
180 185 190
Glu Cys Gln Leu Ile Gln Glu Phe Thr Ser Ala Gln Arg Arg Gly Glu
195 200 205
Val Ser Arg Met Arg Glu Val Ala Ala Val Leu Leu His Phe Lys Gly
210 215 220
Tyr Ser His Cys Ile Asp Val Tyr Ile Lys Gln Cys Gln Glu Gly Ala

225 230 235 240
Tyr Leu Arg Asn Asp Ile Phe Glu Asp Ala Ala Ile Leu Cys Gln Arg
245 250 255
Val Asn Lys Gln Val Gly Asp Ile Phe Ser Asn Pro Glu Ala Val Leu
260 265 270
Ala Lys Leu Ile Gln Asn Val Phe Glu Val Lys Leu Gln Ser Phe Val
275 280 285
Lys Asp Gln Leu Glu Glu Cys Arg Lys Ser Asp Ala Glu Gln Tyr Leu
290 295 300
Lys Ser Leu Tyr Asp Leu Tyr Thr Arg Thr Thr Ser Leu Ser Ser Lys
305 310 315 320
Leu Met Glu Phe Asn Leu Gly Thr Asp Lys Gln Thr Phe Leu Ser Lys
325 330 335

Leu Ile Lys Ser Ile Phe Val Ser Tyr Leu Glu Asn Tyr Ile Glu Val
340 345 350
Glu Ile Gly Tyr Leu Lys Ser Arg Ser Ala Met Ile Leu Gln Arg Tyr
355 360 365
Tyr Asp Ser Lys Asn His Gln Lys Arg Ser Ile Gly Thr Gly Gly Ile
370 375 380
Gln Asp Leu Lys Glu Arg Ile Arg Gln Arg Thr Asn Leu Pro Leu Gly
385 390 395 400
Pro Ser Ile Asp Thr His Gly Glu Thr Phe Leu Ser Gln Glu Val Val
405 410 415
Val Asn Leu Leu Gln Glu Thr Lys Gln Ala Phe Glu Arg Cys His Arg
420 425 430
Leu Ser Asp Pro Ser Asp Leu Pro Arg Asn Ala Phe Arg Ile Phe Thr
435 440 445
Ile Leu Val Glu Phe Leu Cys Ile Glu His Ile Asp Tyr Ala Leu Glu
450 455 460
Thr Gly Leu Ala Gly Ile Pro Ser Ser Asp Ser Arg Asn Ala Asn Leu
465 470 475 480
Tyr Phe Leu Asp Val Val Gln Gln Ala Asn Thr Ile Phe His Leu Phe
485 490 495
Asp Lys Gln Phe Asn Asp His Leu Met Pro Leu Ile Ser Ser Ser Pro
500 505 510
Lys Leu Ser Glu Cys Leu Gln Lys Lys Lys Glu Ile Ile Glu Gln Met
515 520 525
Glu Met Lys Leu Asp Thr Gly Ile Asp Arg Thr Leu Asn Cys Met Ile
530 535 540
Gly Gln Met Lys His Ile Leu Ala Ala Glu Gln Lys Lys Thr Asp Phe
545 550 555 560
Lys Pro Glu Asp Glu Asn Asn Val Leu Ile Gln Tyr Thr Asn Ala Cys
565 570 575
Val Lys Val Cys Ala Tyr Val Arg Lys Gln Val Glu Lys Ile Lys Asn

580 585 590
Ser Met Asp Gly Lys Asn Val Asp Thr Val Leu Met Glu Leu Gly Val
595 600 605
Arg Phe His Arg Leu Thr Tyr Glu His Leu Gln Gln Tyr Ser Tyr Ser
610 615 620
Cys Met Gly Gly Met Leu Ala Ile Cys Asp Val Ala Glu Tyr Arg Lys
625 630 635 640
Cys Ala Lys Asp Phe Lys Ile Pro Met Val Leu His Leu Phe Asp Thr
645 650 655

Leu His Ala Leu Cys Asn Leu Leu Val Val Ala Pro Asp Asn Leu Lys
660 665 670
Gln Val Cys Ser Gly Glu Gln Leu Ala Asn Leu Asp Lys Asn Ile Leu
675 680 685
His Ser Phe Val Gln Leu Arg Ala Asp Tyr Arg Ser Ala Arg Leu Ala
690 695 700
Arg His Phe Ser
705

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2328 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p79 (rexo70)

(ix) FEATURE:
(A) NAME/KEY: Coding Sequence
(B) LOCATION: 298...2256

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

TCAGGTGTAG CTGCATGCTC TGAACACAGA CACTCATGTT CTTCACCTGC TGAGGTAGCC 60
AAGACATTTC CATCAGGCTC TTGGTGTGTC AAGCTTTCTG CTGAGTCTGT GACATTTAGG 120
TCCTGGACAT GAACTACCAT TGTGGGGACC TTTGGGAAGA GGCTCAAAGG GCTTATGTCT 180
TAAATCAATA TTTGTTTCCT TTTTGTCTGG TCACATTTGG GCTGTTCGAG CTGCCATGTC 240
TTGGAGCAGG GTTTGGAGCT AAGACATAGG GGAGTGGGAA CAGCGCTGTC CGCTGCG ATG 300
Met
1

ATT CCC CCG CAG GAG GCT TCC GCT CGG CGG CGG GAG ATC GAG GAC AAG 348
Ile Pro Pro Gln Glu Ala Ser Ala Arg Arg Arg Glu Ile Glu Asp Lys
5 10 15

CTG AAG CAG GAG GAG GAG ACG CTG TCC TTT ATT CGA GAC AGC CTG GAG 396
Leu Lys Gln Glu Glu Glu Thr Leu Ser Phe Ile Arg Asp Ser Leu Glu
20 25 30

AAG AGC GAC CAG CTC ACT AAG AAC ATG GTG TCT ATC CTG TCG TCC TTT 444
Lys Ser Asp Gln Leu Thr Lys Asn Met Val Ser Ile Leu Ser Ser Phe
35 40 45

GAG AGC CGA CTC ATG AAG CTG GAG AAC TCC ATC ATC CCT GTG CAC AAG 492
Glu Ser Arg Leu Met Lys Leu Glu Asn Ser Ile Ile Pro Val His Lys
50 55 60 65

CAG ACA GAG AAC CTA CAG AGG CTG CAG GAG AAT GTC GAA AAG ACC TTA 540
Gln Thr Glu Asn Leu Gln Arg Leu Gln Glu Asn Val Glu Lys Thr Leu
70 75 80

TCC TGC CTG GAC CAT GTT ATC AGC TAT TAC CAC GTA GCC AGC GAC ACG 588
Ser Cys Leu Asp His Val Ile Ser Tyr Tyr His Val Ala Ser Asp Thr
85 90 95

GAG AAG ATC ATC AGA GAG GGC CCC ACA GGT AGG CTG GAA GAA TAC CTG 636
Glu Lys Ile Ile Arg Glu Gly Pro Thr Gly Arg Leu Glu Glu Tyr Leu
100 105 110

GGA AGC ATG GCC AAA ATC CAG AAG GCT GTG GAG TAC TTT CAG GAC AAC 684
Gly Ser Met Ala Lys Ile Gln Lys Ala Val Glu Tyr Phe Gln Asp Asn
115 120 125

AGC CCA GAT AGC CCA GAG CTC AAC AAA GTG AAG CTG CTG TTT GAG CGG 732
Ser Pro Asp Ser Pro Glu Leu Asn Lys Val Lys Leu Leu Phe Glu Arg
130 135 140 145

GGG AAG GAG TCC TTG GAA TCG GAG TTC CGC AGT CTG ATG ACC AGG CAC 780
Gly Lys Glu Ser Leu Glu Ser Glu Phe Arg Ser Leu Met Thr Arg His
150 155 160

AGC AAG GTC ATC TCC CCT GTG CTC GTC CTG GAC CTC ATC AGT GCG GAT 828
Ser Lys Val Ile Ser Pro Val Leu Val Leu Asp Leu Ile Ser Ala Asp
165 170 175

GAC GAG CTG GAG GTC CAG GAG GAC GTG GTC CTG GAG CAC CTG CCT GAG 876
Asp Glu Leu Glu Val Gln Glu Asp Val Val Leu Glu His Leu Pro Glu
180 185 190

AGC GTG CTC CAG GAT GTG ATC CGC ATC TCC CGC TGG CTG GTG GAA TAT 924
Ser Val Leu Gln Asp Val Ile Arg Ile Ser Arg Trp Leu Val Glu Tyr
195 200 205

GGT CGG AAC CAA GAT TTC ATG AAT GTC TAC TAT CAG ATC CGC TCT AGC 972
Gly Arg Asn Gln Asp Phe Met Asn Val Tyr Tyr Gln Ile Arg Ser Ser
210 215 220 225

CAG CTG GAC CGC TCC ATC AAG GGT CTG AAG GAG CAT TTT CGC AAA AGC 1020
Gln Leu Asp Arg Ser Ile Lys Gly Leu Lys Glu His Phe Arg Lys Ser
230 235 240

AGT TCT TCC TCT GGG GTT CCC TAC TCC CCC GCC ATC CCC AAC AAG AGG 1068
Ser Ser Ser Ser Gly Val Pro Tyr Ser Pro Ala Ile Pro Asn Lys Arg
245 250 255

AAA GAC ACG CCT ACC AAG AAG CCC ATC AAG CGG CCA GGG AGA GAT GAC 1116
Lys Asp Thr Pro Thr Lys Lys Pro Ile Lys Arg Pro Gly Arg Asp Asp
260 265 270

ATG CTG GAC GTG GAG ACA GAT GCC TAC ATT CAC TGC GTT AGT GCC TTT 1164
Met Leu Asp Val Glu Thr Asp Ala Tyr Ile His Cys Val Ser Ala Phe
275 280 285

GTC AGG CTG GCA CAG AGT GAA TAC CAG CTG CTG ATG GGC ATC ATT CCC 1212
Val Arg Leu Ala Gln Ser Glu Tyr Gln Leu Leu Met Gly Ile Ile Pro
290 295 300 305

GAG CAT CAC CAG AAG AAA ACC TTC GAC TCC TTG ATA CAG GAT GCC CTA 1260
Glu His His Gln Lys Lys Thr Phe Asp Ser Leu Ile Gln Asp Ala Leu
310 315 320

GAT GGG CTG ATG CTT GAA GGG GAG AAC ATA GTG TCC GCG GCC AGG AAA 1308

Asp Gly Leu Met Leu Glu Gly Glu Asn Ile Val Ser Ala Ala Arg Lys
325 330 335

GCC ATC ATC CGC CAT GAC TTC TCC ACC GTG CTC ACC GTC TTC CCC ATC 1356
Ala Ile Ile Arg His Asp Phe Ser Thr Val Leu Thr Val Phe Pro Ile
340 345 350

CTG CGA CAC CTC AAG CAG ACC AAG CCT GAG TTT GAC CAG GTG CTC CAG 1404
Leu Arg His Leu Lys Gln Thr Lys Pro Glu Phe Asp Gln Val Leu Gln
355 360 365

GGC ACA GCA GCC AGC ACG AAG AAC AAG CTG CCA GGC CTC ATC ACC TCC 1452
Gly Thr Ala Ala Ser Thr Lys Asn Lys Leu Pro Gly Leu Ile Thr Ser
370 375 380 385

ATG GAG ACC ATT GGG GCC AAA GCT CTA GAA GAC TTT GCG GAT AAC ATC 1500
Met Glu Thr Ile Gly Ala Lys Ala Leu Glu Asp Phe Ala Asp Asn Ile
390 395 400

AAG AAT GAT CCA GAC AAG GAG TAC AAC ATG CCT AAA GAT GGC ACC GTT 1548
Lys Asn Asp Pro Asp Lys Glu Tyr Asn Met Pro Lys Asp Gly Thr Val
405 410 415

CAT GAG CTC ACA AGC AAT GCC ATC CTG TTC CTA CAG CAG CTT CTG GAC 1596
His Glu Leu Thr Ser Asn Ala Ile Leu Phe Leu Gln Gln Leu Leu Asp
420 425 430

TTC CAG GAG ACA GCA GGC GCC ATG CTG GCC TCC CAA GAA ACC AGC TCT 1644
Phe Gln Glu Thr Ala Gly Ala Met Leu Ala Ser Gln Glu Thr Ser Ser
435 440 445

TCG GCC ACC AGC TAC AAC TCC GAG TTC AGC AAG CGA CTG CTG AGT ACC 1692
Ser Ala Thr Ser Tyr Asn Ser Glu Phe Ser Lys Arg Leu Leu Ser Thr
450 455 460 465

TAC ATT TGC AAA GTC CTG GGT AAC CTG CAG CTG AAC TTG CTA AGC AAG 1740
Tyr Ile Cys Lys Val Leu Gly Asn Leu Gln Leu Asn Leu Leu Ser Lys
470 475 480

TCC AAG GTG TAT GAG GAT CCA GCT CTG AGC GCC ATC TTC CTA CAC AAC 1788

Ser Lys Val Tyr Glu Asp Pro Ala Leu Ser Ala Ile Phe Leu His Asn
485 490 495

AAC TAC AAC TAC ATC CTC AAG TCC CTG GAG AAG TCT GAG CTG ATC CAG 1836
Asn Tyr Asn Tyr Ile Leu Lys Ser Leu Glu Lys Ser Glu Leu Ile Gln
500 505 510

CTT GTG GCT GTG ACC CAG AAG ACT GCT GAG CGC TCC TAC CGG GAG CAC 1884
Leu Val Ala Val Thr Gln Lys Thr Ala Glu Arg Ser Tyr Arg Glu His
515 520 525

ATT GAG CAG CAG ATC CAG ACC TAC CAG CGC AGC TGG CTA AAG GTG ACT 1932
Ile Glu Gln Gln Ile Gln Thr Tyr Gln Arg Ser Trp Leu Lys Val Thr
530 535 540 545

GAC TAC ATC GCA GAG AAG AAT CTA CCT GTG TTC CAG CCT GGA GTC AAG 1980
Asp Tyr Ile Ala Glu Lys Asn Leu Pro Val Phe Gln Pro Gly Val Lys
550 555 560

CTC CGG GAC AAG GAG CGG CAA ATG ATT AAG GAA CGT TTC AAG GGA TTC 2028
Leu Arg Asp Lys Glu Arg Gln Met Ile Lys Glu Arg Phe Lys Gly Phe
565 570 575

AAT GAT GGG CTC GAA GAA CTG TGC AAG ATT CAG AAG GCC TGG GCC ATC 2076
Asn Asp Gly Leu Glu Glu Leu Cys Lys Ile Gln Lys Ala Trp Ala Ile
580 585 590

CCA GAC ACG GAG CAG AGG GAC AAG ATC CGA CAG GCT CAG AAA AGC ATC 2124
Pro Asp Thr Glu Gln Arg Asp Lys Ile Arg Gln Ala Gln Lys Ser Ile
595 600 605

GTC AAG GAG ACC TAT GGG GCC TTT CTG CAC AGG TAT AGC AGC GTG CCC 2172
Val Lys Glu Thr Tyr Gly Ala Phe Leu His Arg Tyr Ser Ser Val Pro
610 615 620 625

TTC ACC AAA AAC CCG GAG AAG TAC ATC AAG TAC CGT GTG GAG CAG GTG 2220
Phe Thr Lys Asn Pro Glu Lys Tyr Ile Lys Tyr Arg Val Glu Gln Val
630 635 640

GGC GAC ATG ATC GAC CGC CTC TTC GAC ACC TCT GCT TAAGTCGGCC AGCGCT 2272

Gly Asp Met Ile Asp Arg Leu Phe Asp Thr Ser Ala
645 650

TCCGCCCAGT GCCACTGGCG TGCCTAGCAT GTCATCGGAC TCATAAACCA GTGGTA 2328

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 653 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

```
Met Ile Pro Pro Gln Glu Ala Ser Ala Arg Arg Arg Glu Ile Glu Asp
 1               5                  10                  15
Lys Leu Lys Gln Glu Glu Glu Thr Leu Ser Phe Ile Arg Asp Ser Leu
            20                  25                  30
Glu Lys Ser Asp Gln Leu Thr Lys Asn Met Val Ser Ile Leu Ser Ser
        35                  40                  45
Phe Glu Ser Arg Leu Met Lys Leu Glu Asn Ser Ile Ile Pro Val His
    50                  55                  60
Lys Gln Thr Glu Asn Leu Gln Arg Leu Gln Glu Asn Val Glu Lys Thr
65                  70                  75                  80
Leu Ser Cys Leu Asp His Val Ile Ser Tyr Tyr His Val Ala Ser Asp
                85                  90                  95
Thr Glu Lys Ile Ile Arg Glu Gly Pro Thr Gly Arg Leu Glu Glu Tyr
            100                 105                 110
Leu Gly Ser Met Ala Lys Ile Gln Lys Ala Val Glu Tyr Phe Gln Asp
        115                 120                 125
Asn Ser Pro Asp Ser Pro Glu Leu Asn Lys Val Lys Leu Leu Phe Glu
    130                 135                 140
Arg Gly Lys Glu Ser Leu Glu Ser Glu Phe Arg Ser Leu Met Thr Arg
145                 150                 155                 160
His Ser Lys Val Ile Ser Pro Val Leu Val Leu Asp Leu Ile Ser Ala
                165                 170                 175
Asp Asp Glu Leu Glu Val Gln Glu Asp Val Val Leu Glu His Leu Pro
            180                 185                 190
Glu Ser Val Leu Gln Asp Val Ile Arg Ile Ser Arg Trp Leu Val Glu
        195                 200                 205
Tyr Gly Arg Asn Gln Asp Phe Met Asn Val Tyr Tyr Gln Ile Arg Ser
    210                 215                 220
Ser Gln Leu Asp Arg Ser Ile Lys Gly Leu Lys Glu His Phe Arg Lys
225                 230                 235                 240
Ser Ser Ser Ser Ser Gly Val Pro Tyr Ser Pro Ala Ile Pro Asn Lys
                245                 250                 255
Arg Lys Asp Thr Pro Thr Lys Lys Pro Ile Lys Arg Pro Gly Arg Asp
            260                 265                 270
Asp Met Leu Asp Val Glu Thr Asp Ala Tyr Ile His Cys Val Ser Ala
        275                 280                 285
```

Phe Val Arg Leu Ala Gln Ser Glu Tyr Gln Leu Leu Met Gly Ile Ile
290 295 300
Pro Glu His His Gln Lys Lys Thr Phe Asp Ser Leu Ile Gln Asp Ala
305 310 315 320
Leu Asp Gly Leu Met Leu Glu Gly Glu Asn Ile Val Ser Ala Ala Arg
325 330 335
Lys Ala Ile Ile Arg His Asp Phe Ser Thr Val Leu Thr Val Phe Pro
340 345 350
Ile Leu Arg His Leu Lys Gln Thr Lys Pro Glu Phe Asp Gln Val Leu
355 360 365
Gln Gly Thr Ala Ala Ser Thr Lys Asn Lys Leu Pro Gly Leu Ile Thr
370 375 380
Ser Met Glu Thr Ile Gly Ala Lys Ala Leu Glu Asp Phe Ala Asp Asn
385 390 395 400
Ile Lys Asn Asp Pro Asp Lys Glu Tyr Asn Met Pro Lys Asp Gly Thr
405 410 415
Val His Glu Leu Thr Ser Asn Ala Ile Leu Phe Leu Gln Gln Leu Leu
420 425 430
Asp Phe Gln Glu Thr Ala Gly Ala Met Leu Ala Ser Gln Glu Thr Ser
435 440 445

Ser Ser Ala Thr Ser Tyr Asn Ser Glu Phe Ser Lys Arg Leu Leu Ser
450 455 460
Thr Tyr Ile Cys Lys Val Leu Gly Asn Leu Gln Leu Asn Leu Leu Ser
465 470 475 480
Lys Ser Lys Val Tyr Glu Asp Pro Ala Leu Ser Ala Ile Phe Leu His
485 490 495
Asn Asn Tyr Asn Tyr Ile Leu Lys Ser Leu Glu Lys Ser Glu Leu Ile
500 505 510
Gln Leu Val Ala Val Thr Gln Lys Thr Ala Glu Arg Ser Tyr Arg Glu
515 520 525
His Ile Glu Gln Gln Ile Gln Thr Tyr Gln Arg Ser Trp Leu Lys Val
530 535 540
Thr Asp Tyr Ile Ala Glu Lys Asn Leu Pro Val Phe Gln Pro Gly Val
545 550 555 560
Lys Leu Arg Asp Lys Glu Arg Gln Met Ile Lys Glu Arg Phe Lys Gly
565 570 575
Phe Asn Asp Gly Leu Glu Glu Leu Cys Lys Ile Gln Lys Ala Trp Ala
580 585 590
Ile Pro Asp Thr Glu Gln Arg Asp Lys Ile Arg Gln Ala Gln Lys Ser
595 600 605
Ile Val Lys Glu Thr Tyr Gly Ala Phe Leu His Arg Tyr Ser Ser Val
610 615 620
Pro Phe Thr Lys Asn Pro Glu Lys Tyr Ile Lys Tyr Arg Val Glu Gln
625 630 635 640

Val Gly Asp Met Ile Asp Arg Leu Phe Asp Thr Ser Ala
645 650

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2496 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p84 (rexo84)

(ix) FEATURE:
(A) NAME/KEY: Coding Sequence
(B) LOCATION: 156...2303

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

GGCACGAGGC GCAATGCAGC GCTCGGCCCC GGCGCAGGCG TTTGGGTGTT GCTCCCGCCC 60
CGCTTCCTCT ACCGCTTCTC CACCGGGCTC GGGTGGGGCC GGGAGGCGGC GAGTGACAGC 120
CACTGCGGGC CACGGGAGCA GGGCGGGTGG CAGCC ATG TCG GAC AGC GGG GCG 173
Met Ser Asp Ser Gly Ala
1 5

AGC CGC CTG CGG AGG CAG CTG GAG TCG GGG GGC TTC GAG GCG CGG CTG 221
Ser Arg Leu Arg Arg Gln Leu Glu Ser Gly Gly Phe Glu Ala Arg Leu
10 15 20

TAC GTG AAG CAA CTG TCG CAG CAG TCG GAC GGC GAC CGC GAC CTG CAG 269
Tyr Val Lys Gln Leu Ser Gln Gln Ser Asp Gly Asp Arg Asp Leu Gln
25 30 35

GAG CAC CGA CAG CGG GTG CAG GCG CTG GCG GAG GAG ACG GCG CAG AAC 317
Glu His Arg Gln Arg Val Gln Ala Leu Ala Glu Glu Thr Ala Gln Asn
40 45 50

CTG AAG CGC AAC GTC TAC CAG AAC TAC CGG CAG TTC ATC GAG ACG GCG 365
Leu Lys Arg Asn Val Tyr Gln Asn Tyr Arg Gln Phe Ile Glu Thr Ala
55 60 65 70

CGC GAG ATC TCC TAC CTG GAG AGC GAG ATG TAC CAG CTG AGC CAC CTG 413
Arg Glu Ile Ser Tyr Leu Glu Ser Glu Met Tyr Gln Leu Ser His Leu
75 80 85

CTG ACG GAG CAG AAG AGC AGT CTG GAG AGC ATC CCG CTG GCA CTG CTG 461
Leu Thr Glu Gln Lys Ser Ser Leu Glu Ser Ile Pro Leu Ala Leu Leu
90 95 100

CCC GCC GCT GCC GCG GGC GCA TCC ACG GGT GAG GAC ACG GCG GGC GCG 509
Pro Ala Ala Ala Ala Gly Ala Ser Thr Gly Glu Asp Thr Ala Gly Ala
105 110 115

GGA CCG CGG GAG CGC GGG GCG GCC CAG GCG GGC TTT CTT CCG GGG CCG 557
Gly Pro Arg Glu Arg Gly Ala Ala Gln Ala Gly Phe Leu Pro Gly Pro
120 125 130

GCC GGA GTC CCT CGC GAG GGC CCC GGG ACG GGA GAG GAG GGC AAG CAG 605
Ala Gly Val Pro Arg Glu Gly Pro Gly Thr Gly Glu Glu Gly Lys Gln
135 140 145 150

CGA ACG CTC ACC ACG CTG CTG GAG AAG GTG GAG GGC TGC AGG GAC CTG 653
Arg Thr Leu Thr Thr Leu Leu Glu Lys Val Glu Gly Cys Arg Asp Leu
155 160 165

CTG GAG ACA CCA GGT CAG TAC CTT GTG TAC AAC GGG GAC CTG GTG GAA 701
Leu Glu Thr Pro Gly Gln Tyr Leu Val Tyr Asn Gly Asp Leu Val Glu
170 175 180

TAC GAG GCA GAC CAT ATG GCC CAG CTG CAG CGA GTG CAT GGC TTC CTC 749
Tyr Glu Ala Asp His Met Ala Gln Leu Gln Arg Val His Gly Phe Leu
185 190 195

ATG AAC GAC TGT CTG CTG GTG GCC ACT TGG CTA CCA CAA CGG CGA GGC 797
Met Asn Asp Cys Leu Leu Val Ala Thr Trp Leu Pro Gln Arg Arg Gly
200 205 210

ATG TAC CGC TAC AAC GCA CTC TAC CCA CTG GAC CGC CTG GCT GTG GTC 845
Met Tyr Arg Tyr Asn Ala Leu Tyr Pro Leu Asp Arg Leu Ala Val Val
215 220 225 230

AAC GTC AAA GAC AAT CCA CCT ATG AAA GAC ATG TTC AAG CTG CTC ATG 893

Asn Val Lys Asp Asn Pro Pro Met Lys Asp Met Phe Lys Leu Leu Met
235 240 245

TTC CCT GAG AGC CGA ATC TTT CAA GCG GAA AAT GCC AAG ATT AAA CGC 941
Phe Pro Glu Ser Arg Ile Phe Gln Ala Glu Asn Ala Lys Ile Lys Arg
250 255 260

GAG TGG CTG GAA GTG TTG GAG GAA ACC AAG AGG GCG CTC AGC GAC AAG 989

Glu Trp Leu Glu Val Leu Glu Glu Thr Lys Arg Ala Leu Ser Asp Lys
265 270 275

AGG AGA CGG GAG CAG GAG GAG GCA GCC GCC TTG CGT GCG CCA CCA CCG 1037
Arg Arg Arg Glu Gln Glu Glu Ala Ala Ala Leu Arg Ala Pro Pro Pro
280 285 290

GTC ACT TCC AAG GGC AGC AAC CCG TTT GAG GAT GAG GCC GAG GAG GAA 1085
Val Thr Ser Lys Gly Ser Asn Pro Phe Glu Asp Glu Ala Glu Glu Glu
295 300 305 310

CTG GCC ACC CCG GAG GCA GAG GAG GAA AAG GTT GAC CTT TCC ATG GAG 1133
Leu Ala Thr Pro Glu Ala Glu Glu Glu Lys Val Asp Leu Ser Met Glu
315 320 325

TGG ATC CAG GAG TTG CCG GAA GAC CTG GAT GTT TGT ATT GCG CAG AGG 1181
Trp Ile Gln Glu Leu Pro Glu Asp Leu Asp Val Cys Ile Ala Gln Arg
330 335 340

GAC TTT GAG GGT GCC GTG GAC TTG CTG GAC AAA TTA AAT CAC TAT CTT 1229
Asp Phe Glu Gly Ala Val Asp Leu Leu Asp Lys Leu Asn His Tyr Leu
345 350 355

GAA GAT AAG CCC AGC CCA CCT TCT GTG AAA GAG CTG AGG GCC AAA GTG 1277
Glu Asp Lys Pro Ser Pro Pro Ser Val Lys Glu Leu Arg Ala Lys Val
360 365 370

GAT GAA CGA GTG CGA CAG CTC ACC GAG GTG CTT GTG TTT GAG CTC TCC 1325
Asp Glu Arg Val Arg Gln Leu Thr Glu Val Leu Val Phe Glu Leu Ser
375 380 385 390

CCG GAT CGC TCT CTG AGA GGT GGC CCT AAG GCT ACT CGA AGG GCA GTG 1373
Pro Asp Arg Ser Leu Arg Gly Gly Pro Lys Ala Thr Arg Arg Ala Val
395 400 405

TCT CAA CTG ATC CGT CTC GGC CAG TGC ACT AAG GCT TGT GAG CTG TTT 1421

```
Ser Gln Leu Ile Arg Leu Gly Gln Cys Thr Lys Ala Cys Glu Leu Phe
            410                 415                 420

CTG AGG AAC AGG GCG GCA GCT GTG CAT ACT GCC ATC CGC CAG CTT CGA   1469

Leu Arg Asn Arg Ala Ala Ala Val His Thr Ala Ile Arg Gln Leu Arg
        425                 430                 435

ATT GAG GGC GCC ACT CTG CTC TAT ATT CAC AAG CTG TGC CAT GTC TTC   1517
Ile Glu Gly Ala Thr Leu Leu Tyr Ile His Lys Leu Cys His Val Phe
    440                 445                 450

TTT ACC AGC CTC CTA GAG ACT GCA CGG GAG TTT GAG ACA GAC TTT GCA   1565
Phe Thr Ser Leu Leu Glu Thr Ala Arg Glu Phe Glu Thr Asp Phe Ala
455                 460                 465                 470

GGC ACG GAC AGT GGC TGC TAC TCT GCC TTT GTG GTC TGG GCA AGG TCT   1613
Gly Thr Asp Ser Gly Cys Tyr Ser Ala Phe Val Val Trp Ala Arg Ser
                475                 480                 485

GCC ATG GGC ATG TTC GTG GAT GCT TTC AGC AAG CAG GTT TTT GAC AGC   1661
Ala Met Gly Met Phe Val Asp Ala Phe Ser Lys Gln Val Phe Asp Ser
            490                 495                 500

AAG GAG AGC CTG TCC ACT GCT GCC GAG TGT GTG AAG GTA GCC AAG GAG   1709
Lys Glu Ser Leu Ser Thr Ala Ala Glu Cys Val Lys Val Ala Lys Glu
        505                 510                 515

CAC TGC CAG CAG CTG GGA GAG ATT GGG CTG GAT CTC ACC TTC ATC ATC   1757
His Cys Gln Gln Leu Gly Glu Ile Gly Leu Asp Leu Thr Phe Ile Ile
    520                 525                 530

CAT GCC CTC CTG GTG AAG GAC ATC CAG GGG GCC TTG CTC AGT TAC AAG   1805
His Ala Leu Leu Val Lys Asp Ile Gln Gly Ala Leu Leu Ser Tyr Lys
535                 540                 545                 550

GAG ATT ATC ATT GAA GCC ACC AAG CAC CGA AAC TCG GAG GAG ATG TGG   1853
Glu Ile Ile Ile Glu Ala Thr Lys His Arg Asn Ser Glu Glu Met Trp
                555                 560                 565

CGT CGG ATG AAC CTG ATG ACT CCT GAG GCC CTG GGC AAG CTC AAG GAG   1901
Arg Arg Met Asn Leu Met Thr Pro Glu Ala Leu Gly Lys Leu Lys Glu
            570                 575                 580

GAG ATG AGA AGT TGC GGG GTC AGT AAC TTT GAG CAG TAT ACG GGG GAT   1949
```

Glu Met Arg Ser Cys Gly Val Ser Asn Phe Glu Gln Tyr Thr Gly Asp
585 590 595

GAC TGC TGG GTG AAC CTG AGC TAC ACT GTG GTA GCC TTC ACC AAG CAG 1997
Asp Cys Trp Val Asn Leu Ser Tyr Thr Val Val Ala Phe Thr Lys Gln
600 605 610

ACC ATG GGC TTC CTG GAG GAG GCA CTG AAA CTG TAC TTC CCA GAG CTA 2045
Thr Met Gly Phe Leu Glu Glu Ala Leu Lys Leu Tyr Phe Pro Glu Leu
615 620 625 630

CAC ATG GTG CTC CTG GAG AGT CTG GTG GAA GTC ATA CTG GTT GCT GTG 2093
His Met Val Leu Leu Glu Ser Leu Val Glu Val Ile Leu Val Ala Val
635 640 645

CAG CAT GTG GAC TAC AGC CTG CGC TGT GAG CAG GAC CCA GAG AAG AAG 2141
Gln His Val Asp Tyr Ser Leu Arg Cys Glu Gln Asp Pro Glu Lys Lys
650 655 660

ACT TTC ATC CGG CAG AAC GCA TCC TTC CTT TAC GAC ACT GTC CTC CCA 2189
Thr Phe Ile Arg Gln Asn Ala Ser Phe Leu Tyr Asp Thr Val Leu Pro
665 670 675

GTG GTG GAG AGG AGG TTT GAG GAA GGT GTA GGG AAG CCT GCC AAG CAG 2237
Val Val Glu Arg Arg Phe Glu Glu Gly Val Gly Lys Pro Ala Lys Gln
680 685 690

CTG CAG GAC CTT CGG AAT GCA TCG AGA CTC CTG CGG GTG AAT CCT GAG 2285
Leu Gln Asp Leu Arg Asn Ala Ser Arg Leu Leu Arg Val Asn Pro Glu
695 700 705 710

AGC ACC ACG TCT GTG GTC TGAGGCTCTG GTTCGATGCT GTGTGTGCGT CTGTCTGT 2341
Ser Thr Thr Ser Val Val
715

CTGTCTGTCT GTATGTATGT ATGTATGTAT GTATGTCTGT ACACACACAT GTACTACAGA 2401
TGCATTGTTT GTATTCACAT TACACAATAT CAACACATTC CTCAGACACA AACAGCATAT 2461
AAAAGTGCCC TCTTAAAAAT GCAGTCAAAA AAAAA 2496

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 716 amino acids

(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

```
Met Ser Asp Ser Gly Ala Ser Arg Leu Arg Arg Gln Leu Glu Ser Gly
 1               5                  10                  15
Gly Phe Glu Ala Arg Leu Tyr Val Lys Gln Leu Ser Gln Gln Ser Asp
            20                  25                  30
Gly Asp Arg Asp Leu Gln Glu His Arg Gln Arg Val Gln Ala Leu Ala
        35                  40                  45
Glu Glu Thr Ala Gln Asn Leu Lys Arg Asn Val Tyr Gln Asn Tyr Arg
    50                  55                  60
Gln Phe Ile Glu Thr Ala Arg Glu Ile Ser Tyr Leu Glu Ser Glu Met
65                  70                  75                  80
Tyr Gln Leu Ser His Leu Leu Thr Glu Gln Lys Ser Ser Leu Glu Ser
                85                  90                  95
Ile Pro Leu Ala Leu Leu Pro Ala Ala Ala Ala Gly Ala Ser Thr Gly
            100                 105                 110
Glu Asp Thr Ala Gly Ala Gly Pro Arg Glu Arg Gly Ala Ala Gln Ala
        115                 120                 125
Gly Phe Leu Pro Gly Pro Ala Gly Val Pro Arg Glu Gly Pro Gly Thr
    130                 135                 140
Gly Glu Glu Gly Lys Gln Arg Thr Leu Thr Thr Leu Leu Glu Lys Val
145                 150                 155                 160
Glu Gly Cys Arg Asp Leu Leu Glu Thr Pro Gly Gln Tyr Leu Val Tyr
                165                 170                 175
Asn Gly Asp Leu Val Glu Tyr Glu Ala Asp His Met Ala Gln Leu Gln
            180                 185                 190
Arg Val His Gly Phe Leu Met Asn Asp Cys Leu Leu Val Ala Thr Trp
        195                 200                 205
Leu Pro Gln Arg Arg Gly Met Tyr Arg Tyr Asn Ala Leu Tyr Pro Leu
    210                 215                 220
Asp Arg Leu Ala Val Val Asn Val Lys Asp Asn Pro Pro Met Lys Asp
225                 230                 235                 240
Met Phe Lys Leu Leu Met Phe Pro Glu Ser Arg Ile Phe Gln Ala Glu
                245                 250                 255
Asn Ala Lys Ile Lys Arg Glu Trp Leu Glu Val Leu Glu Glu Thr Lys
            260                 265                 270
Arg Ala Leu Ser Asp Lys Arg Arg Arg Glu Gln Glu Glu Ala Ala Ala
        275                 280                 285
Leu Arg Ala Pro Pro Pro Val Thr Ser Lys Gly Ser Asn Pro Phe Glu
    290                 295                 300
```

Asp Glu Ala Glu Glu Glu Leu Ala Thr Pro Glu Ala Glu Glu Glu Lys
305 310 315 320
Val Asp Leu Ser Met Glu Trp Ile Gln Glu Leu Pro Glu Asp Leu Asp
325 330 335
Val Cys Ile Ala Gln Arg Asp Phe Glu Gly Ala Val Asp Leu Leu Asp
340 345 350
Lys Leu Asn His Tyr Leu Glu Asp Lys Pro Ser Pro Pro Ser Val Lys
355 360 365
Glu Leu Arg Ala Lys Val Asp Glu Arg Val Arg Gln Leu Thr Glu Val
370 375 380
Leu Val Phe Glu Leu Ser Pro Asp Arg Ser Leu Arg Gly Gly Pro Lys
385 390 395 400
Ala Thr Arg Arg Ala Val Ser Gln Leu Ile Arg Leu Gly Gln Cys Thr
405 410 415
Lys Ala Cys Glu Leu Phe Leu Arg Asn Arg Ala Ala Ala Val His Thr
420 425 430
Ala Ile Arg Gln Leu Arg Ile Glu Gly Ala Thr Leu Leu Tyr Ile His
435 440 445
Lys Leu Cys His Val Phe Phe Thr Ser Leu Leu Glu Thr Ala Arg Glu
450 455 460
Phe Glu Thr Asp Phe Ala Gly Thr Asp Ser Gly Cys Tyr Ser Ala Phe
465 470 475 480
Val Val Trp Ala Arg Ser Ala Met Gly Met Phe Val Asp Ala Phe Ser
485 490 495
Lys Gln Val Phe Asp Ser Lys Glu Ser Leu Ser Thr Ala Ala Glu Cys
500 505 510

Val Lys Val Ala Lys Glu His Cys Gln Gln Leu Gly Glu Ile Gly Leu
515 520 525
Asp Leu Thr Phe Ile Ile His Ala Leu Leu Val Lys Asp Ile Gln Gly
530 535 540
Ala Leu Leu Ser Tyr Lys Glu Ile Ile Ile Glu Ala Thr Lys His Arg
545 550 555 560
Asn Ser Glu Glu Met Trp Arg Arg Met Asn Leu Met Thr Pro Glu Ala
565 570 575
Leu Gly Lys Leu Lys Glu Glu Met Arg Ser Cys Gly Val Ser Asn Phe
580 585 590
Glu Gln Tyr Thr Gly Asp Asp Cys Trp Val Asn Leu Ser Tyr Thr Val
595 600 605
Val Ala Phe Thr Lys Gln Thr Met Gly Phe Leu Glu Glu Ala Leu Lys
610 615 620
Leu Tyr Phe Pro Glu Leu His Met Val Leu Leu Glu Ser Leu Val Glu
625 630 635 640
Val Ile Leu Val Ala Val Gln His Val Asp Tyr Ser Leu Arg Cys Glu
645 650 655

Gln Asp Pro Glu Lys Lys Thr Phe Ile Arg Gln Asn Ala Ser Phe Leu
660 665 670
Tyr Asp Thr Val Leu Pro Val Val Glu Arg Arg Phe Glu Glu Gly Val
675 680 685
Gly Lys Pro Ala Lys Gln Leu Gln Asp Leu Arg Asn Ala Ser Arg Leu
690 695 700
Leu Arg Val Asn Pro Glu Ser Thr Thr Ser Val Val
705 710 715

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 3059 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p96 (rsec15)

(ix) FEATURE:
(A) NAME/KEY: Coding Sequence
(B) LOCATION: 341...2806

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

CCGCGTCGAC CCGGCACAAA CACACCATGC ACCCTGACAG TAAATTTATA AAAAATTTTT
60
TTCAACTATA GCACAAAAAA TGTGTATCAC TTAACAGGGA TGACAAATGG CTGTCACTTC 120
AGTCACTATA ATGCACAATA TATATATGCC TTCTACTTAT GAAGCACGTT TACTGGAAAA 180
CAACTGTTAT GCAGACGGCA TCCTCATTTT TCTTATGTTT GGTCTCTTGT CCCTTGAGAG 240
ATCATGTCCA GTAAGGGATC TACAACAGTT CCTTGTGTGT GTTAACAATG ATGAAATCAC 300
AATTGATGTG TTTTCCTGAG TCTGTCCCCA CAGTTAAACA ATG CCT TTC TCC CCG 355
Met Pro Phe Ser Pro
1 5

GGG CGC CGC GCC CGG CCG GCG CCT CCG CTT CCA GCC AAG ATG GCG GAG 403

Gly Arg Arg Ala Arg Pro Ala Pro Pro Leu Pro Ala Lys Met Ala Glu
10 15 20

AGC GGC GAG GCT CTG GGT ACG GTC CCG GAG CAC GAG CGG ATC TTG CAG 451
Ser Gly Glu Ala Leu Gly Thr Val Pro Glu His Glu Arg Ile Leu Gln
25 30 35

GAG ATC GAA AGC ACG GAC ACC GCC TGC GTA GGG CCC ACC CTT CGG TCT 499
Glu Ile Glu Ser Thr Asp Thr Ala Cys Val Gly Pro Thr Leu Arg Ser
40 45 50

GTG TAT GAT GGT CAG CCA AAT GCA CAC AAG AAG TTC ATG GAA AAG CTA 547
Val Tyr Asp Gly Gln Pro Asn Ala His Lys Lys Phe Met Glu Lys Leu
55 60 65

GAT GCC TGC ATC CGC AAC CAT GAC AAG GAG ATT GAG AAA ATG TGT AAC 595
Asp Ala Cys Ile Arg Asn His Asp Lys Glu Ile Glu Lys Met Cys Asn
70 75 80 85

TTC CAT CAC CAG GGC TTT GTA GAT GCT ATC ACA GAG CTC CTC AAA GTA 643
Phe His His Gln Gly Phe Val Asp Ala Ile Thr Glu Leu Leu Lys Val
90 95 100

AGG GCG GAC GCA GAA AAG CTG AAG GTC CAG GTT ACT GAT ACC AAC CGA 691
Arg Ala Asp Ala Glu Lys Leu Lys Val Gln Val Thr Asp Thr Asn Arg
105 110 115

AGG TTC CAA GAT GCT GGA AAA GAG GTG ATA GAA CAA ACA GAA GAT ATT 739
Arg Phe Gln Asp Ala Gly Lys Glu Val Ile Glu Gln Thr Glu Asp Ile
120 125 130

ATT CGG TGT AGA ATT CAG CAG AGA AAT ATT ACA ACC GTA GTA GAG AAA 787
Ile Arg Cys Arg Ile Gln Gln Arg Asn Ile Thr Thr Val Val Glu Lys
135 140 145

TTG CAG TTA TGC CTG CCA GTG TTG GAG ATG TAC AGT AAA CTG AAG GAA 835
Leu Gln Leu Cys Leu Pro Val Leu Glu Met Tyr Ser Lys Leu Lys Glu
150 155 160 165

CAG ATG AGC ATG CAG AGG TAT TAT TCT GCA CTT AAA ACA ATG GAA CAG 883
Gln Met Ser Met Gln Arg Tyr Tyr Ser Ala Leu Lys Thr Met Glu Gln
170 175 180

TTA GAG AAC GTA TAC TTT CCT CGG GTT AGC CAG TAC CGC TTC TGT CAG 931
Leu Glu Asn Val Tyr Phe Pro Arg Val Ser Gln Tyr Arg Phe Cys Gln

185 190 195

CTC ATG ATG GAC ACA CTT CCT AAA CTC CGG GAG GAT ATC AAA GAC ATC 979
Leu Met Met Asp Thr Leu Pro Lys Leu Arg Glu Asp Ile Lys Asp Ile
200 205 210

TCC ATG TCT GAC CTC AAG GAC TTT CTG GAA AGC ATT CGA AAG CAT TCT 1027
Ser Met Ser Asp Leu Lys Asp Phe Leu Glu Ser Ile Arg Lys His Ser
215 220 225

GAC AAA ATA GGG GAA ACA GCC ATG AAA CAG GCA CAA CAG CAG AAG AGC 1075
Asp Lys Ile Gly Glu Thr Ala Met Lys Gln Ala Gln Gln Gln Lys Ser
230 235 240 245

TTC AGT ATT GCT GTA CAG AAG CAA ACC AAT ATG AGG TTT GGG AAA AAT 1123
Phe Ser Ile Ala Val Gln Lys Gln Thr Asn Met Arg Phe Gly Lys Asn
250 255 260

ATG CAT GTA AAC AAT GAC AGG ACT CTA GAG GAA AAG AGT GAC ATC ATA 1171
Met His Val Asn Asn Asp Arg Thr Leu Glu Glu Lys Ser Asp Ile Ile
265 270 275

CTG AAG CAC ACA CTT GAG GAG GAG GCC GAG AAT GAC GAG GAG GTC TTA 1219
Leu Lys His Thr Leu Glu Glu Glu Ala Glu Asn Asp Glu Glu Val Leu
280 285 290

ACT GTT CAA GAT CTC GTT GAC TTT TCC CCT GTT TAC CGA TGC TCA CAC 1267
Thr Val Gln Asp Leu Val Asp Phe Ser Pro Val Tyr Arg Cys Ser His
295 300 305

ATT TAT TCT GCT TTG GGT GAT GAA GAA ACA TTT GAA AAT TAT TAC CGG 1315
Ile Tyr Ser Ala Leu Gly Asp Glu Glu Thr Phe Glu Asn Tyr Tyr Arg
310 315 320 325

AAG CAA AGG AAG AAG CAG GCG CGC CTG GTT CTG CAG CCG CAG TCG AGT 1363
Lys Gln Arg Lys Lys Gln Ala Arg Leu Val Leu Gln Pro Gln Ser Ser
330 335 340

GTG CAT GAA ACA GTT GAT GGC TAT AGA AGA TAT TTC ACT CAG ATT GTA 1411
Val His Glu Thr Val Asp Gly Tyr Arg Arg Tyr Phe Thr Gln Ile Val
345 350 355

GGG TTC TTT GTT GTG GAA GAT CAC ATT TTA CAT GTG ACC CAA GGA TTA 1459
Gly Phe Phe Val Val Glu Asp His Ile Leu His Val Thr Gln Gly Leu

535 540 545

TGC TTA CTG AAC CTC ATT AGA AAA CCT CAC ATA GGT TTG ACA GAG CTG 2035
Cys Leu Leu Asn Leu Ile Arg Lys Pro His Ile Gly Leu Thr Glu Leu
550 555 560 565

GTG CAA ATT ATC ATA AAC ACA ACA CAC CTG GAG CAG GCT TGC AAA TAC 2083

Val Gln Ile Ile Ile Asn Thr Thr His Leu Glu Gln Ala Cys Lys Tyr
570 575 580

CTG GAG GAC TTT ATA ACT AAC ATT ACA AAT ATT TCT CAA GAA ACC GTT 2131
Leu Glu Asp Phe Ile Thr Asn Ile Thr Asn Ile Ser Gln Glu Thr Val
585 590 595

CAC ACC ACA AGA CTT TAT GGA CTT TCT ACT TTT AAG GAT GCA CGA CAT 2179
His Thr Thr Arg Leu Tyr Gly Leu Ser Thr Phe Lys Asp Ala Arg His
600 605 610

GCA GCG GAA GGA GAA ATA TAT ACC AAA CTC AAT CAG AAG ATT GAT GAG 2227
Ala Ala Glu Gly Glu Ile Tyr Thr Lys Leu Asn Gln Lys Ile Asp Glu
615 620 625

TTT GTC CAG CTG GCC GAC TAC GAC TGG ACC ATG GCT GAG TCG GAT GGG 2275
Phe Val Gln Leu Ala Asp Tyr Asp Trp Thr Met Ala Glu Ser Asp Gly
630 635 640 645

AGA GCA AGT GGT TAT TTA ATG GAT CTT ATT AAT TTT TTG AGA AGC ATC 2323
Arg Ala Ser Gly Tyr Leu Met Asp Leu Ile Asn Phe Leu Arg Ser Ile
650 655 660

TTT CAA GTA TTT ACC CAC TTG CCT GGG AAA GTT GCC CAG ACA GCT TGC 2371
Phe Gln Val Phe Thr His Leu Pro Gly Lys Val Ala Gln Thr Ala Cys
665 670 675

ATG TCA GCC TGC CAA CAT CTG TCC ACA TCC TTG ATG CAG ATG CTC CTG 2419
Met Ser Ala Cys Gln His Leu Ser Thr Ser Leu Met Gln Met Leu Leu
680 685 690

GAC AGC GAG TTA AAG CAG ATC AGC ATG GGG GCC GTA CAG CAG TTT AAC 2467
Asp Ser Glu Leu Lys Gln Ile Ser Met Gly Ala Val Gln Gln Phe Asn
695 700 705

CTA GAC GTC ATA CAG TGC GAA TTG TTT GCC AGC TCT GAG CCT GTG CCA 2515
Leu Asp Val Ile Gln Cys Glu Leu Phe Ala Ser Ser Glu Pro Val Pro

710 715 720 725

GGA TTC CAA GGG GAC ACC CTG CAG CTG GCC TTC ATT GAC CTC AGA CAG 2563

Gly Phe Gln Gly Asp Thr Leu Gln Leu Ala Phe Ile Asp Leu Arg Gln
730 735 740

CTC CTT GAC TTG TTT ATG GTT TGG GAC TGG TCT ACT TAC CTG GCT GAC 2611
Leu Leu Asp Leu Phe Met Val Trp Asp Trp Ser Thr Tyr Leu Ala Asp
745 750 755

TAT GGG CAG CCA GCT TCC AAG TAC CTC CGG GTG AAC CCA CAC GCC GCC 2659
Tyr Gly Gln Pro Ala Ser Lys Tyr Leu Arg Val Asn Pro His Ala Ala
760 765 770

CTT ACG CTT TTG GAG AAG ATG AAG GAC ACC AGT AAG AAG AAT AAC ATA 2707
Leu Thr Leu Leu Glu Lys Met Lys Asp Thr Ser Lys Lys Asn Asn Ile
775 780 785

TTT GCC CAG TTC CGG AAG AAC GAC CGG GAC AGA CAG AAG CTG ATC GAG 2755
Phe Ala Gln Phe Arg Lys Asn Asp Arg Asp Arg Gln Lys Leu Ile Glu
790 795 800 805

ACA GTG GTG AAA CAG CTC AGA GGC TTG GTG ACC GGT ATG TCC CAG CAC 2803
Thr Val Val Lys Gln Leu Arg Gly Leu Val Thr Gly Met Ser Gln His
810 815 820

ATG TAGACCAGAT CCATGCCCGA GTGCTTCTCT GTGGCCAGCA CCGGTCATGA GACAAT 2862
Met

AATTTGTTTA CAGAAGCCAA AAACTGTAGT AGAGGAAAGA TACTAATGAG GGCTTAAACA 2922
ATAAGGACAG CAAACATCAT TTGTATGGAC TTTTAATAAC TGAATACTAT TTTATATATA 2982
AAAATGTAAC ATTAATTTTT TCCAATTTTA GAAGAAAAGT CAAAAGTGTA ATATATAAAC 3042
CCAATAAATT GTGTATG 3059

(2) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 822 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

```
Met Pro Phe Ser Pro Gly Arg Arg Ala Arg Pro Ala Pro Pro Leu Pro
 1               5                  10                  15
Ala Lys Met Ala Glu Ser Gly Glu Ala Leu Gly Thr Val Pro Glu His
            20                  25                  30
Glu Arg Ile Leu Gln Glu Ile Glu Ser Thr Asp Thr Ala Cys Val Gly
        35                  40                  45
Pro Thr Leu Arg Ser Val Tyr Asp Gly Gln Pro Asn Ala His Lys Lys
    50                  55                  60
Phe Met Glu Lys Leu Asp Ala Cys Ile Arg Asn His Asp Lys Glu Ile
65                  70                  75                  80
Glu Lys Met Cys Asn Phe His His Gln Gly Phe Val Asp Ala Ile Thr
                85                  90                  95
Glu Leu Leu Lys Val Arg Ala Asp Ala Glu Lys Leu Lys Val Gln Val
            100                 105                 110
Thr Asp Thr Asn Arg Arg Phe Gln Asp Ala Gly Lys Glu Val Ile Glu
        115                 120                 125
Gln Thr Glu Asp Ile Ile Arg Cys Arg Ile Gln Gln Arg Asn Ile Thr
    130                 135                 140
Thr Val Val Glu Lys Leu Gln Leu Cys Leu Pro Val Leu Glu Met Tyr
145                 150                 155                 160
Ser Lys Leu Lys Glu Gln Met Ser Met Gln Arg Tyr Tyr Ser Ala Leu
                165                 170                 175
Lys Thr Met Glu Gln Leu Glu Asn Val Tyr Phe Pro Arg Val Ser Gln
            180                 185                 190
Tyr Arg Phe Cys Gln Leu Met Met Asp Thr Leu Pro Lys Leu Arg Glu
        195                 200                 205
Asp Ile Lys Asp Ile Ser Met Ser Asp Leu Lys Asp Phe Leu Glu Ser
    210                 215                 220
Ile Arg Lys His Ser Asp Lys Ile Gly Glu Thr Ala Met Lys Gln Ala
225                 230                 235                 240

Gln Gln Gln Lys Ser Phe Ser Ile Ala Val Gln Lys Gln Thr Asn Met
                245                 250                 255
Arg Phe Gly Lys Asn Met His Val Asn Asn Asp Arg Thr Leu Glu Glu
            260                 265                 270
Lys Ser Asp Ile Ile Leu Lys His Thr Leu Glu Glu Glu Ala Glu Asn
        275                 280                 285
Asp Glu Glu Val Leu Thr Val Gln Asp Leu Val Asp Phe Ser Pro Val
    290                 295                 300
Tyr Arg Cys Ser His Ile Tyr Ser Ala Leu Gly Asp Glu Glu Thr Phe
305                 310                 315                 320
Glu Asn Tyr Tyr Arg Lys Gln Arg Lys Lys Gln Ala Arg Leu Val Leu
                325                 330                 335
```

Gln Pro Gln Ser Ser Val His Glu Thr Val Asp Gly Tyr Arg Arg Tyr
340 345 350
Phe Thr Gln Ile Val Gly Phe Phe Val Val Glu Asp His Ile Leu His
355 360 365
Val Thr Gln Gly Leu Val Thr Arg Ala Tyr Thr Asp Glu Leu Trp Asn
370 375 380
Met Ala Leu Ser Lys Ile Ile Ala Val Leu Arg Ala His Ser Ser Tyr
385 390 395 400
Cys Thr Asp Pro Asp Leu Val Leu Glu Leu Lys Xaa Leu Ile Val Ile
405 410 415
Phe Ala Asp Thr Leu Gln Gly Tyr Gly Phe Ser Val Asn Arg Leu Phe
420 425 430
Asp Leu Leu Phe Glu Ile Arg Asp Gln Tyr Asn Glu Thr Leu Leu Lys
435 440 445
Lys Trp Ala Gly Ile Phe Arg Asp Ile Phe Glu Glu Asp Asn Tyr Ser
450 455 460
Pro Ile Pro Ile Gly Ser Glu Glu Glu Tyr Lys Met Val Ile Ser Lys
465 470 475 480
Phe Pro Phe Gln Asp Pro Asp Leu Glu Lys Gln Ser Phe Pro Lys Lys
485 490 495
Phe Pro Met Ser Gln Ser Val Pro Leu Ile Tyr Ile Gln Val Lys Glu
500 505 510
Phe Ile Tyr Ala Ser Leu Lys Phe Ser Glu Ser Leu His Arg Ser Ser
515 520 525
Thr Glu Ile Asp Asp Met Leu Arg Lys Ser Thr Asn Leu Leu Leu Thr
530 535 540
Arg Ile Leu Ser Ser Cys Leu Leu Asn Leu Ile Arg Lys Pro His Ile
545 550 555 560

Gly Leu Thr Glu Leu Val Gln Ile Ile Ile Asn Thr Thr His Leu Glu
565 570 575
Gln Ala Cys Lys Tyr Leu Glu Asp Phe Ile Thr Asn Ile Thr Asn Ile
580 585 590
Ser Gln Glu Thr Val His Thr Thr Arg Leu Tyr Gly Leu Ser Thr Phe
595 600 605
Lys Asp Ala Arg His Ala Ala Glu Gly Glu Ile Tyr Thr Lys Leu Asn
610 615 620
Gln Lys Ile Asp Glu Phe Val Gln Leu Ala Asp Tyr Asp Trp Thr Met
625 630 635 640
Ala Glu Ser Asp Gly Arg Ala Ser Gly Tyr Leu Met Asp Leu Ile Asn
645 650 655
Phe Leu Arg Ser Ile Phe Gln Val Phe Thr His Leu Pro Gly Lys Val
660 665 670
Ala Gln Thr Ala Cys Met Ser Ala Cys Gln His Leu Ser Thr Ser Leu
675 680 685

Met Gln Met Leu Leu Asp Ser Glu Leu Lys Gln Ile Ser Met Gly Ala
690 695 700
Val Gln Gln Phe Asn Leu Asp Val Ile Gln Cys Glu Leu Phe Ala Ser
705 710 715 720
Ser Glu Pro Val Pro Gly Phe Gln Gly Asp Thr Leu Gln Leu Ala Phe
725 730 735
Ile Asp Leu Arg Gln Leu Leu Asp Leu Phe Met Val Trp Asp Trp Ser
740 745 750
Thr Tyr Leu Ala Asp Tyr Gly Gln Pro Ala Ser Lys Tyr Leu Arg Val
755 760 765
Asn Pro His Ala Ala Leu Thr Leu Leu Glu Lys Met Lys Asp Thr Ser
770 775 780
Lys Lys Asn Asn Ile Phe Ala Gln Phe Arg Lys Asn Asp Arg Asp Arg
785 790 795 800
Gln Lys Leu Ile Glu Thr Val Val Lys Gln Leu Arg Gly Leu Val Thr
805 810 815
Gly Met Ser Gln His Met
820

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 4358 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA to mRNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:
(C) INDIVIDUAL ISOLATE: p102 (rsec5)

(ix) FEATURE:
(A) NAME/KEY: Coding Sequence
(B) LOCATION: 200...2971

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

110

ACTGCTGCGG CCCGGAGCGG GTTGGCCCGG ACCTGACGCC GCCTGCAAGC TGCAGGACAG 60

AGGGCTGGAG ATGGCAGATC CCAGGAGCTA GCAGCCAGCC CAGCCGAATG GTGTCTCCAC 120

CTGGAGTGCA GGAGAGAGAG ACTGAAAACC AAAAAGGTTG CTTTTATAAC TGGAACAGGA 180

GTTTGCTGCT CAAAGTACA ATG TCT CGA TCC CGG CAG CCT CCA CTT GTG ACA 232
Met Ser Arg Ser Arg Gln Pro Pro Leu Val Thr
1 5 10

GGC ATC TCT CCA AAT GAA GGG ATT CCT TGG ACC AAA GTC ACA ATT AGA 280
Gly Ile Ser Pro Asn Glu Gly Ile Pro Trp Thr Lys Val Thr Ile Arg
15 20 25

GGG GAG AAT CTG GGT ACT GGT CCC ACT GAC CTT ATA GGC TTG ACA ATT 328
Gly Glu Asn Leu Gly Thr Gly Pro Thr Asp Leu Ile Gly Leu Thr Ile
30 35 40

TGT GGA CAT AAT TGC CTC CTC ACG GCA GAA TGG ATG TCT GCA AGT AAA 376
Cys Gly His Asn Cys Leu Leu Thr Ala Glu Trp Met Ser Ala Ser Lys
45 50 55

ATT GTC TGT CGA GTG GGA CAA GCC AAA AAT GAC AAA GGA GAC ATT ATT 424
Ile Val Cys Arg Val Gly Gln Ala Lys Asn Asp Lys Gly Asp Ile Ile
60 65 70 75

GTC ACA ACC AAG TCA GGG GGC AGA GGA ACC TCA ACT GTC TCT TTT AAG 472
Val Thr Thr Lys Ser Gly Gly Arg Gly Thr Ser Thr Val Ser Phe Lys
80 85 90

CTA CTC AAA CCT GAA AAA ATA GGC ATT TTG GAT CAG TCT GCA GTG TGG 520
Leu Leu Lys Pro Glu Lys Ile Gly Ile Leu Asp Gln Ser Ala Val Trp
95 100 105

GTG GAT GAG ATG AAT TAT TAT GAT ATG CGG ACT GAC AGG AAT AAG GGG 568
Val Asp Glu Met Asn Tyr Tyr Asp Met Arg Thr Asp Arg Asn Lys Gly
110 115 120

ATT CCC CCC TTG TCA CTT CGT CCT GCG AAT CCT CTC GGC ATT GAA ATT 616
Ile Pro Pro Leu Ser Leu Arg Pro Ala Asn Pro Leu Gly Ile Glu Ile
125 130 135

GAG AAG TGT AAA CTT CCT CAG AAG AAC TTA GAA GTG TTA TTC CAT GGC 664
Glu Lys Cys Lys Leu Pro Gln Lys Asn Leu Glu Val Leu Phe His Gly
140 145 150 155

ATG AGT GCT GAT TTT ACG AGT GAG AAT TTT TCA GCA GCC TGG TAT CTC 712

Met Ser Ala Asp Phe Thr Ser Glu Asn Phe Ser Ala Ala Trp Tyr Leu
160 165 170

ATA GAG AAC CAC TCC AAC ACC AGT TTT GAG CAG CTC AAG ATG GCA GTT 760
Ile Glu Asn His Ser Asn Thr Ser Phe Glu Gln Leu Lys Met Ala Val
175 180 185

ACC AAC CTC AAA AGG CAG GCC AAC AAG AAG AGC GAG GGT AGT CTA GCG 808
Thr Asn Leu Lys Arg Gln Ala Asn Lys Lys Ser Glu Gly Ser Leu Ala
190 195 200

TAC GTG AAG GGT GGC CTC AGT ACC TTC TTT GAA GCT CAA GAT GCT CTC 856
Tyr Val Lys Gly Gly Leu Ser Thr Phe Phe Glu Ala Gln Asp Ala Leu
205 210 215

TCA GCT ATC CAT CAA AAA CTA GAA GCA GAC GGA ACA GAA AAA GTA GAA 904
Ser Ala Ile His Gln Lys Leu Glu Ala Asp Gly Thr Glu Lys Val Glu
220 225 230 235

GGA TCC ATG ACA CAG AAA TTG GAG AAT GTC CTC AAC AGA GCA AGT AAT 952
Gly Ser Met Thr Gln Lys Leu Glu Asn Val Leu Asn Arg Ala Ser Asn
240 245 250

ACT GCT GAC ACA TTG TTT CAA GAA GTG TTA GGT CGG AAA GAC AAG GCA 1000
Thr Ala Asp Thr Leu Phe Gln Glu Val Leu Gly Arg Lys Asp Lys Ala
255 260 265

GAT TCC ACT AGG AAT GCA CTC AAC GTG CTT CAG CGG TTT AAA TTT CTC 1048
Asp Ser Thr Arg Asn Ala Leu Asn Val Leu Gln Arg Phe Lys Phe Leu
270 275 280

TTC AAC CTT CCT CTC AAT ATC AAA CGG AAC ATT CAA AAG GGG GAT TAT 1096
Phe Asn Leu Pro Leu Asn Ile Lys Arg Asn Ile Gln Lys Gly Asp Tyr
285 290 295

GAT GTG GTT ATT AAT GAT TAT GAA AAA GCC AAA TCG CTC TTT GGG AAA 1144
Asp Val Val Ile Asn Asp Tyr Glu Lys Ala Lys Ser Leu Phe Gly Lys
300 305 310 315

ACG GAG GTG CAA GTT TTC AAG AAA TAT TAT GCT GAA GTA GAG GCA GGA 1192
Thr Glu Val Gln Val Phe Lys Lys Tyr Tyr Ala Glu Val Glu Ala Gly
320 325 330

ATT GAA GAT CTA AGA GAG TTA CTT CTA AAG AAA CTG CTC GAG ACT CCG 1240
Ile Glu Asp Leu Arg Glu Leu Leu Leu Lys Lys Leu Leu Glu Thr Pro

335 340 345

TCA ACC TTA CAT GAC CAG AAG CGT TAC ATA AGG TAT CTT TCT GAC CTC 1288
Ser Thr Leu His Asp Gln Lys Arg Tyr Ile Arg Tyr Leu Ser Asp Leu
350 355 360

CAT GCT CCT GGT GAT CCT GCT TGG CAG TGT ATC GGA GCT CAG CAC AAG 1336
His Ala Pro Gly Asp Pro Ala Trp Gln Cys Ile Gly Ala Gln His Lys
365 370 375

TGG ACC CTC AAA CTC ATG CAA GAC TGC AAA GAA GGC CAC ATG AAG AGC 1384
Trp Thr Leu Lys Leu Met Gln Asp Cys Lys Glu Gly His Met Lys Ser
380 385 390 395

CTG AAA GGT AAC CCA GGC CCA CAC AGC CCC ATG CTT GAC CTA GAT AAT 1432

Leu Lys Gly Asn Pro Gly Pro His Ser Pro Met Leu Asp Leu Asp Asn
400 405 410

GAT GCC CGC CCC TCT GTG TTG GGC CAT CTC AGT CAG ACA GCA TCA CTG 1480
Asp Ala Arg Pro Ser Val Leu Gly His Leu Ser Gln Thr Ala Ser Leu
415 420 425

AAG AGA GGC AGC AGC TTC CAG TCT GGT CGA GAT GAC ACA TGG AGG TAC 1528
Lys Arg Gly Ser Ser Phe Gln Ser Gly Arg Asp Asp Thr Trp Arg Tyr
430 435 440

AAG ACG CCC CAC AGA GTG GCA TTT GTT GAA AAA TTA ACG AAG CTT GTG 1576
Lys Thr Pro His Arg Val Ala Phe Val Glu Lys Leu Thr Lys Leu Val
445 450 455

TTA AGT CAG CTG CCT AAC TTC TGG AAA CTC TGG ATT TCA TAT GTT AAT 1624
Leu Ser Gln Leu Pro Asn Phe Trp Lys Leu Trp Ile Ser Tyr Val Asn
460 465 470 475

GGA AGT CTG TTC AGT GAG ACA GCT GAG AAG TCA GGC CAG ATT GAA AGA 1672
Gly Ser Leu Phe Ser Glu Thr Ala Glu Lys Ser Gly Gln Ile Glu Arg
480 485 490

TCA AAG AAT GTG AGG CAA AGA CAA AAT GAT TTC AAG AAA ATG ATT CAA 1720
Ser Lys Asn Val Arg Gln Arg Gln Asn Asp Phe Lys Lys Met Ile Gln
495 500 505

GAA GTA ATG CAC TCC CTG GTG AAG TTG ATC CGG GGA GCC CTG CTC CCA 1768
Glu Val Met His Ser Leu Val Lys Leu Ile Arg Gly Ala Leu Leu Pro

510 515 520

TTC AGC CTC CGA GAA GGG GAT GGG AGA CAG TAT GGC GGC TGG GAG GTG 1816
Phe Ser Leu Arg Glu Gly Asp Gly Arg Gln Tyr Gly Gly Trp Glu Val
525 530 535

CAG GCA GAG CTC TCG GGG CAG TGG CTC GCA CAC GTT ATC CAG ACC ATA 1864
Gln Ala Glu Leu Ser Gly Gln Trp Leu Ala His Val Ile Gln Thr Ile
540 545 550 555

AGG CTG ACA TAT GAA TCA CTG ACC GCT CTG GAG ATT CCC AAT GAC ATG 1912
Arg Leu Thr Tyr Glu Ser Leu Thr Ala Leu Glu Ile Pro Asn Asp Met
560 565 570

TTA CAG ATT ATC CAG GAC CTG ATT TTG GAT CTC CGT ATA CAT TGC ATA 1960
Leu Gln Ile Ile Gln Asp Leu Ile Leu Asp Leu Arg Ile His Cys Ile
575 580 585

ATG GTG ACG TTG CAA CAT ACA GCT GAA GAG ATA AAG AGA TTA GCT GAA 2008
Met Val Thr Leu Gln His Thr Ala Glu Glu Ile Lys Arg Leu Ala Glu
590 595 600

AAA GAA GAT TGG ATT GTT GAT AAC GAA GGA CTG ACT TCC CTA CCA TGT 2056
Lys Glu Asp Trp Ile Val Asp Asn Glu Gly Leu Thr Ser Leu Pro Cys
605 610 615

CAG TTT GAA CAG AGC ATT GTT CAC TCC CTG CAG TCG TTG AAG GGT GTT 2104
Gln Phe Glu Gln Ser Ile Val His Ser Leu Gln Ser Leu Lys Gly Val
620 625 630 635

GTG GAT TGC AAA CCT GGA GAA GCC AGT GTC TTT CAG CAG CCT AAA ACC 2152
Val Asp Cys Lys Pro Gly Glu Ala Ser Val Phe Gln Gln Pro Lys Thr
640 645 650

CAG GAG GAG GTT TGC CAG TTG TGC ATC AGT ATC ATG CAG GTT TTT ATA 2200
Gln Glu Glu Val Cys Gln Leu Cys Ile Ser Ile Met Gln Val Phe Ile
655 660 665

TAC TGC CTG GAA CAA CTG AGC ACC AAG CCT GAT GCG GAC ATA GAT ACT 2248
Tyr Cys Leu Glu Gln Leu Ser Thr Lys Pro Asp Ala Asp Ile Asp Thr
670 675 680

ACT CAT CTT TCT GTT GAT GTT TCT TCT CCT GAT TTG TTT GGA AGC ATC 2296
Thr His Leu Ser Val Asp Val Ser Ser Pro Asp Leu Phe Gly Ser Ile

685 690 695

CAT GAA GAC TTC GGT TTG ACT TCA GAG CAG AGG CTT TTG ATA GTC CTG 2344
His Glu Asp Phe Gly Leu Thr Ser Glu Gln Arg Leu Leu Ile Val Leu
700 705 710 715

AGT AAT TGC TGC TAT TTA GAA CGT CAC ACC TTC CTA AAC ATA GCA GAA 2392
Ser Asn Cys Cys Tyr Leu Glu Arg His Thr Phe Leu Asn Ile Ala Glu
720 725 730

CAT TTT GAA AAG CAC AAC TTC CAG GGA ATA GAA AAA ATA ACA CAG GTT 2440
His Phe Glu Lys His Asn Phe Gln Gly Ile Glu Lys Ile Thr Gln Val
735 740 745

AGT ATG GCA TCA CTG AAA GAA CTG GAT CAA CGA CTC TTT GAA AAT TAC 2488
Ser Met Ala Ser Leu Lys Glu Leu Asp Gln Arg Leu Phe Glu Asn Tyr
750 755 760

ATT GAG CTA AAA GCA GAT CCT ATT GTT GGA TCC TTG GAA ACT GGG ATA 2536
Ile Glu Leu Lys Ala Asp Pro Ile Val Gly Ser Leu Glu Thr Gly Ile
765 770 775

TAT GCA GGC TAT TTT GAT TGG AAA GAC TGT CTG CCT CCA GCA GGT GTC 2584
Tyr Ala Gly Tyr Phe Asp Trp Lys Asp Cys Leu Pro Pro Ala Gly Val
780 785 790 795

AGA AAC TAT TTA AAA GAA GCA CTG GTG AAT ATA ATT GCT GTG CAT GCA 2632
Arg Asn Tyr Leu Lys Glu Ala Leu Val Asn Ile Ile Ala Val His Ala
800 805 810

GAG GTG TTC ACT ATT TCC AAA GAA CTG GTG CCC CGG GTC CTG GCC AGA 2680
Glu Val Phe Thr Ile Ser Lys Glu Leu Val Pro Arg Val Leu Ala Arg
815 820 825

GTG ATA GAA GCA GTC TCT GAA GAG CTG AGC CGG CTG ATG CAG TGT GTC 2728
Val Ile Glu Ala Val Ser Glu Glu Leu Ser Arg Leu Met Gln Cys Val
830 835 840

TCA TCC TTC AGC AGA AAT GGA GCG CTG CAG GCC AGA CTT GAA ATC TGT 2776
Ser Ser Phe Ser Arg Asn Gly Ala Leu Gln Ala Arg Leu Glu Ile Cys
845 850 855

GCT CTG AGG GAC ACT GTA GCC ATT TAC CTG ACC CCG GAG AGC AGG TCT 2824
Ala Leu Arg Asp Thr Val Ala Ile Tyr Leu Thr Pro Glu Ser Arg Ser

860 865 870 875

AGT TTT AAA CAG GCC CTG GAG GCC CTG CCT CAG CTT GCA AGT GGT GCA 2872

Ser Phe Lys Gln Ala Leu Glu Ala Leu Pro Gln Leu Ala Ser Gly Ala
880 885 890

GAC AAA AAG CTA CTG GAA GAG CTG CTC AAC AAG TTC AAG AGC AGT ATG 2920
Asp Lys Lys Leu Leu Glu Glu Leu Leu Asn Lys Phe Lys Ser Ser Met
895 900 905

CAC TTG CAG CTC ACC TGC TTC CAA GCT GCG TCT CCA ACA GTG ATG AAG 2968
His Leu Gln Leu Thr Cys Phe Gln Ala Ala Ser Pro Thr Val Met Lys
910 915 920

ACA TAGACACAGA CAGAGATCCC AGTCCAAGCA CTGCATTTAC CTTCTCTCTT TTCCCC 3027
Thr

AGCATGGTGG TGCAGAAAGA TGTTGATGGG TATTTAATTT CAGCCGATTT AGACTACCAT 3087
ACAATTTTGT TATTACTAGC TTTGGTCCTG TAGCATACTC TTCAAAATGT TTTTTCTTAG 3147
CTCTATGTTT CTTGGTGTGA GTTTTGAGAG CTTCTCCAGC ATGGCCCAAA GCGGCCNATG 3207
GTGTGTGTGA ATGTGCTNCG CAGTGGCGCT CTACCTGGCC TCAGTGTTGG CAGTTTCCAG 3267
CCCAGGGGAG GATATGAAGT CACAGCTTTT GGAGCTGTCA TAAACTTTAA ACCCACCATT 3327
TCAAACAAGT GGTTCTAGGT GCGCTCTCTC TCTCTCTCTC TCTCTCTCTC TCTCTCTCTC 3387
TGTAAAGAAA AATATAAAAA TGTTAAAATC TGTGATGCAG AAGTCCCTGG ATGAACTCTG 3447
AATTTCATAG TCTGGCTTTC ATTTTTCCCA GTGTTCAACA CGGAAGCTTC TGGTTCTCAC 3507
CCTTAAGTTG ATGCATCGTT GTGGGGAGGG TTTACAAGGA CCTGAATGTG GAGGCCCTGT 3567
CACACCCGCA AGCCCTGTGG CAGGCTTGTG GTCTTCAATG CAACCTAAAG ATTAAGCCAG 3627
GCTCCTCCCC TCCCGCAGGT TACTCCCCTC TGCTACTTTC CACACTTCGA AATGTCTTGC 3687
TCCATAGCTG GAAAGATGGT GCCCTGGCAC AGGCTGTGTT TTGTAAAGAT TAGAGGTGCC 3747
TCGGTGACCA GGCATTGAGC AGTGACTCAC TGCTCACTGG CTGGCACAGT AGAATCTGGT 3807
CACTGCGACC TGCAAGCAGC TTTTACCTCA CTGCATCTGA CCCTAGCTTC AGCTCTGGTT 3867
CACTCCAGAC AGATCTGTGG CGCCTTTCTT TCAGTTGACA AAATTCCTGT CACTTTTAGT 3927
TCAGGTAATT CCAGAGCACA GCATATGCAC ACTATGGATT ATTTGAGGTT AATAACAGTG 3987
TGTTTATTTA TCACAGTAAC TGGAAGTACA AATTTAATCC TTTGTTTGCA AAGTATGTAT 4047
GTACAGCATT GTCTCCTCAG TGCACTGGTA TTACATCTGG CATAGCCAAA CTGAATTCCA 4107
AGGCAGAAGT ACACAACTAT TGGTTGTTTA AACACCTAAC AAATACACTA CACAAAGCCA 4167
GTAGTCTTCC TTCTCTGTAA AACCTCTAAG TGTCTTTATT TCACCATTTT TTATTAGCTC 4227
TGTAATTGTT TATATTCCTA GTTTTAAAAT CCAAAATAAA TAGTGGTGTT CTCTCTTTAA 4287
AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 4347
AAAAAAAAAA A 4358

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 924 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

```
Met Ser Arg Ser Arg Gln Pro Pro Leu Val Thr Gly Ile Ser Pro Asn
 1               5                  10                  15
Glu Gly Ile Pro Trp Thr Lys Val Thr Ile Arg Gly Glu Asn Leu Gly
            20                  25                  30
Thr Gly Pro Thr Asp Leu Ile Gly Leu Thr Ile Cys Gly His Asn Cys
        35                  40                  45
Leu Leu Thr Ala Glu Trp Met Ser Ala Ser Lys Ile Val Cys Arg Val
    50                  55                  60
Gly Gln Ala Lys Asn Asp Lys Gly Asp Ile Ile Val Thr Thr Lys Ser
65                  70                  75                  80
Gly Gly Arg Gly Thr Ser Thr Val Ser Phe Lys Leu Leu Lys Pro Glu
                85                  90                  95
Lys Ile Gly Ile Leu Asp Gln Ser Ala Val Trp Val Asp Glu Met Asn
            100                 105                 110
Tyr Tyr Asp Met Arg Thr Asp Arg Asn Lys Gly Ile Pro Pro Leu Ser
        115                 120                 125
Leu Arg Pro Ala Asn Pro Leu Gly Ile Glu Ile Glu Lys Cys Lys Leu
    130                 135                 140
Pro Gln Lys Asn Leu Glu Val Leu Phe His Gly Met Ser Ala Asp Phe
145                 150                 155                 160
Thr Ser Glu Asn Phe Ser Ala Ala Trp Tyr Leu Ile Glu Asn His Ser
                165                 170                 175
Asn Thr Ser Phe Glu Gln Leu Lys Met Ala Val Thr Asn Leu Lys Arg
            180                 185                 190
Gln Ala Asn Lys Lys Ser Glu Gly Ser Leu Ala Tyr Val Lys Gly Gly
        195                 200                 205
Leu Ser Thr Phe Phe Glu Ala Gln Asp Ala Leu Ser Ala Ile His Gln
    210                 215                 220
Lys Leu Glu Ala Asp Gly Thr Glu Lys Val Glu Gly Ser Met Thr Gln
225                 230                 235                 240
Lys Leu Glu Asn Val Leu Asn Arg Ala Ser Asn Thr Ala Asp Thr Leu
                245                 250                 255
Phe Gln Glu Val Leu Gly Arg Lys Asp Lys Ala Asp Ser Thr Arg Asn
            260                 265                 270
Ala Leu Asn Val Leu Gln Arg Phe Lys Phe Leu Phe Asn Leu Pro Leu
        275                 280                 285
```

Asn Ile Lys Arg Asn Ile Gln Lys Gly Asp Tyr Asp Val Val Ile Asn
290 295 300
Asp Tyr Glu Lys Ala Lys Ser Leu Phe Gly Lys Thr Glu Val Gln Val
305 310 315 320
Phe Lys Lys Tyr Tyr Ala Glu Val Glu Ala Gly Ile Glu Asp Leu Arg
325 330 335
Glu Leu Leu Leu Lys Lys Leu Leu Glu Thr Pro Ser Thr Leu His Asp
340 345 350
Gln Lys Arg Tyr Ile Arg Tyr Leu Ser Asp Leu His Ala Pro Gly Asp
355 360 365
Pro Ala Trp Gln Cys Ile Gly Ala Gln His Lys Trp Thr Leu Lys Leu
370 375 380
Met Gln Asp Cys Lys Glu Gly His Met Lys Ser Leu Lys Gly Asn Pro
385 390 395 400
Gly Pro His Ser Pro Met Leu Asp Leu Asp Asn Asp Ala Arg Pro Ser
405 410 415
Val Leu Gly His Leu Ser Gln Thr Ala Ser Leu Lys Arg Gly Ser Ser
420 425 430
Phe Gln Ser Gly Arg Asp Asp Thr Trp Arg Tyr Lys Thr Pro His Arg
435 440 445
Val Ala Phe Val Glu Lys Leu Thr Lys Leu Val Leu Ser Gln Leu Pro
450 455 460
Asn Phe Trp Lys Leu Trp Ile Ser Tyr Val Asn Gly Ser Leu Phe Ser
465 470 475 480
Glu Thr Ala Glu Lys Ser Gly Gln Ile Glu Arg Ser Lys Asn Val Arg
485 490 495
Gln Arg Gln Asn Asp Phe Lys Lys Met Ile Gln Glu Val Met His Ser
500 505 510

Leu Val Lys Leu Ile Arg Gly Ala Leu Leu Pro Phe Ser Leu Arg Glu
515 520 525
Gly Asp Gly Arg Gln Tyr Gly Gly Trp Glu Val Gln Ala Glu Leu Ser
530 535 540
Gly Gln Trp Leu Ala His Val Ile Gln Thr Ile Arg Leu Thr Tyr Glu
545 550 555 560
Ser Leu Thr Ala Leu Glu Ile Pro Asn Asp Met Leu Gln Ile Ile Gln
565 570 575
Asp Leu Ile Leu Asp Leu Arg Ile His Cys Ile Met Val Thr Leu Gln
580 585 590
His Thr Ala Glu Glu Ile Lys Arg Leu Ala Glu Lys Glu Asp Trp Ile
595 600 605
Val Asp Asn Glu Gly Leu Thr Ser Leu Pro Cys Gln Phe Glu Gln Ser
610 615 620
Ile Val His Ser Leu Gln Ser Leu Lys Gly Val Val Asp Cys Lys Pro
625 630 635 640

Gly Glu Ala Ser Val Phe Gln Gln Pro Lys Thr Gln Glu Glu Val Cys
645 650 655
Gln Leu Cys Ile Ser Ile Met Gln Val Phe Ile Tyr Cys Leu Glu Gln
660 665 670
Leu Ser Thr Lys Pro Asp Ala Asp Ile Asp Thr Thr His Leu Ser Val
675 680 685
Asp Val Ser Ser Pro Asp Leu Phe Gly Ser Ile His Glu Asp Phe Gly
690 695 700
Leu Thr Ser Glu Gln Arg Leu Leu Ile Val Leu Ser Asn Cys Cys Tyr
705 710 715 720
Leu Glu Arg His Thr Phe Leu Asn Ile Ala Glu His Phe Glu Lys His
725 730 735
Asn Phe Gln Gly Ile Glu Lys Ile Thr Gln Val Ser Met Ala Ser Leu
740 745 750
Lys Glu Leu Asp Gln Arg Leu Phe Glu Asn Tyr Ile Glu Leu Lys Ala
755 760 765
Asp Pro Ile Val Gly Ser Leu Glu Thr Gly Ile Tyr Ala Gly Tyr Phe
770 775 780
Asp Trp Lys Asp Cys Leu Pro Pro Ala Gly Val Arg Asn Tyr Leu Lys
785 790 795 800
Glu Ala Leu Val Asn Ile Ile Ala Val His Ala Glu Val Phe Thr Ile
805 810 815
Ser Lys Glu Leu Val Pro Arg Val Leu Ala Arg Val Ile Glu Ala Val
820 825 830

Ser Glu Glu Leu Ser Arg Leu Met Gln Cys Val Ser Ser Phe Ser Arg
835 840 845
Asn Gly Ala Leu Gln Ala Arg Leu Glu Ile Cys Ala Leu Arg Asp Thr
850 855 860
Val Ala Ile Tyr Leu Thr Pro Glu Ser Arg Ser Ser Phe Lys Gln Ala
865 870 875 880
Leu Glu Ala Leu Pro Gln Leu Ala Ser Gly Ala Asp Lys Lys Leu Leu
885 890 895
Glu Glu Leu Leu Asn Lys Phe Lys Ser Ser Met His Leu Gln Leu Thr
900 905 910
Cys Phe Gln Ala Ala Ser Pro Thr Val Met Lys Thr
915 920

IT IS CLAIMED:

1. A substantially purified polypeptide selected from the group consisting of

a. SA-17S p71, having a molecular weight of about 71 kD and having the sequence of SEQ ID NO:54;

b. SA-17S p79, having a molecular weight of about 79 kD and having the sequence of SEQ ID NO:56;

c. SA-17S p84, having a molecular weight of about 84 kD and having the sequence of SEQ ID NO:58;

d. SA-17S p96, having a molecular weight of about 96 kD and having the sequence of SEQ ID NO:60;

e. SA-17S p102, having a molecular weight of about 102 kD and having the sequence of SEQ ID NO:62;

f. SA-17S p106, having a molecular weight of about 106 kD and characterized by sequences selected from the group consisting of SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, and SEQ ID NO:52; and

g. a polypeptide having (i) at least 60% sequence identity with a selected one of the SA-17S polypeptides (a)-(f), and (ii) the property of the selected polypeptide to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

2. The polypeptide of claim 1, which is selected from the group consisting of (a)-(e) and (h),

h. a polypeptide having (i) at least 60% sequence identity with a selected one of the SA-17S polypeptides (a)-(e), and (ii) the property of the selected peptide to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

3. The polypeptide of claim 2, which is polypeptide (a) or a polypeptide having (i) at least 60% sequence identity with polypeptide (a) and the property of the polypeptide (a) to form an SC complex-binding SA-17S complex when

combined stoichiometrically with other polypeptide components of the SA-17S complex.

4. The polypeptide of claim 2, which is polypeptide (b) or a polypeptide having (i) at least 60% sequence identity with polypeptide (b) and the property of the polypeptide (b) to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

5. The polypeptide of claim 2, which is polypeptide (c) or a polypeptide having (i) at least 60% sequence identity with polypeptide (c) and the property of the polypeptide (c) to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

6. The polypeptide of claim 2, which is polypeptide (d) or a polypeptide having (i) at least 60% sequence identity with polypeptide (d) and the property of the polypeptide (d) to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

7. The polypeptide of claim 2, which is polypeptide (e) or a polypeptide having (i) at least 60% sequence identity with polypeptide (e) and the property of the polypeptide (e) to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

8. A substantially purified polynucleotide encoding one of the polypeptides (a)-(g) in claim 1, said polynucleotide being selected from the group consisting of

a. a polynucleotide having the sequence SEQ ID NO:53, which encodes the SA-17S p71 protein;

b. a polynucleotide having the sequence SEQ ID NO:55, which encodes the SA-17S p79 protein;

c. a polynucleotide having the sequence SEQ ID NO:57, which encodes the SA-17S p84 protein;

d. a polynucleotide sequence having the sequence SEQ ID NO:59, which encodes the SA-17S p96 protein;

e. a polynucleotide having the sequence SEQ ID NO:61, which encodes the SA-17S p102 protein; and

f. a polynucleotide (i) having at least 60% sequence identity with a selected one of the SA-17S polynucleotides (a)-(e), and (ii) encoding a polypeptide having the property of the polypeptide encoded by the selected polynucleotide to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

9. The polynucleotide of claim 8, which is polynucleotide (a) or a polynucleotide having (i) at least 60% sequence identity with polynucleotide (a) and the property of the SA-17S p71 polypeptide encoded by polynucleotide (a) to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

10. The polynucleotide of claim 8, which is polynucleotide (b) or a polynucleotide having (i) at least 60% sequence identity with polynucleotide (b) and the property of the SA-17S p79 polypeptide encoded by polynucleotide (b) to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

11. The polynucleotide of claim 8, which is polynucleotide (c) or a polynucleotide having (i) at least 60% sequence identity with polynucleotide (c) and the property of the SA-17S p84 polypeptide encoded by polynucleotide (c) to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

12. The polynucleotide of claim 8, which is polynucleotide (d) or a polynucleotide having (i) at least 60% sequence identity with polynucleotide (d) and the property of the SA-17S p96 polypeptide encoded by polynucleotide (d) to form

an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

13. The polynucleotide of claim 8, which is polynucleotide (e) or a polynucleotide having (i) at least 60% sequence identity with polynucleotide (e) and the property of the SA-17S p102 polypeptide encoded by polynucleotide (e) to form an SC complex-binding SA-17S complex when combined stoichiometrically with other polypeptide components of the SA-17S complex.

14. A method of identifying a compound capable of modulating secretion of secretory vesicles, comprising

contacting a secretion associated 17S (SA-17S) complex containing a polypeptide from claim 1 with a syntaxin-containing (SC) complex in the presence and absence of a test compound,

measuring the effect of the test compound on the extent of binding between the SA-17S and the SC complexes, and

identifying said compound as effective if its measured effect on the extent of binding is above a threshold level.

15. The method of claim 14, wherein said SA-17S complex binds to the 7S SC complex or the 20S SC complex.

16. The method of claim 14, wherein said secretory vesicles are neurotransmitter-containing synaptic vesicles.

17. The method of claim 16, wherein the test compound is effective to enhance binding of the SC complex with said SA-17S complex.

18. The method of claim 16, wherein the test compound is effective to inhibit binding of the SC complex with said SA-17S complex.

19. A method for treating an affective disorder comprising administering to a subject in need of such treatment an effective amount of a compound identified in claim 17.

20. A method for treating a neurodegenerative disease comprising administering to a subject in need of such treatment an effective amount of a compound identified in claim 17.

21. A method for treating schizophrenia comprising administering to a subject in need of such treatment an effective amount of a compound identified in claim 18.

Fig. 1A

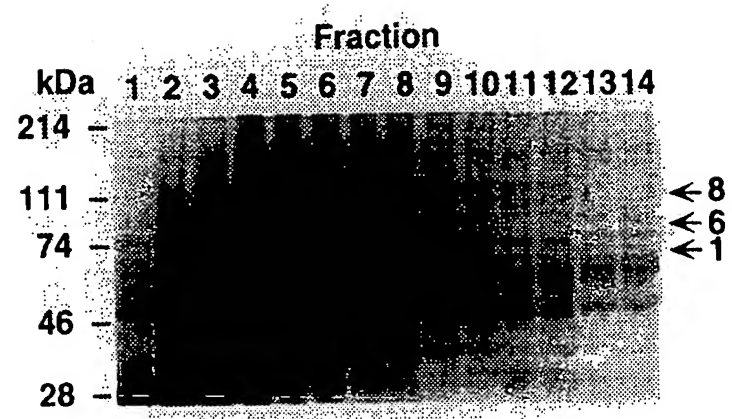


Fig. 1B

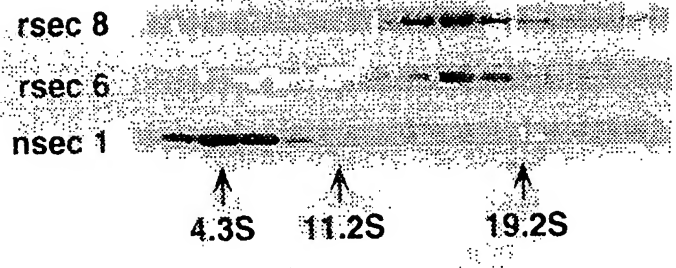


Fig. 1C

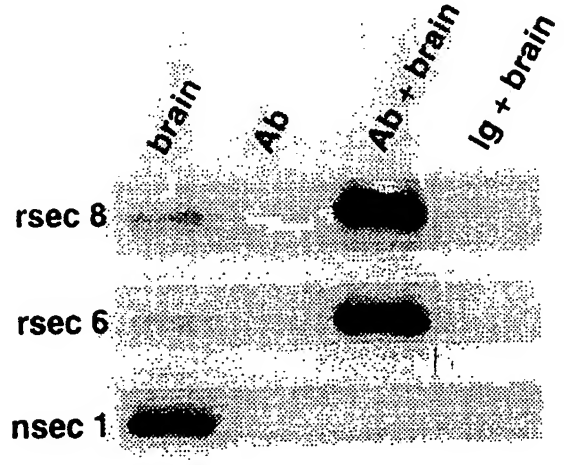


Fig. 2A

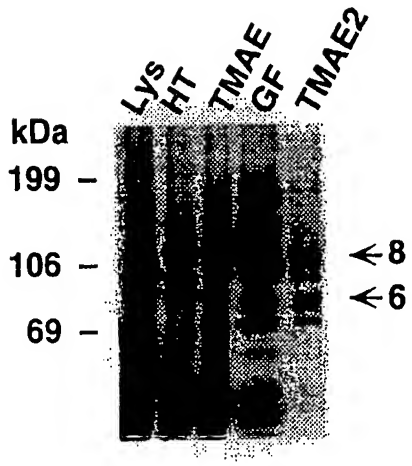


Fig. 2B

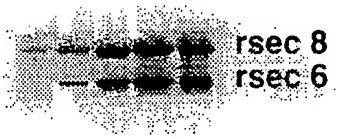


Fig. 2C

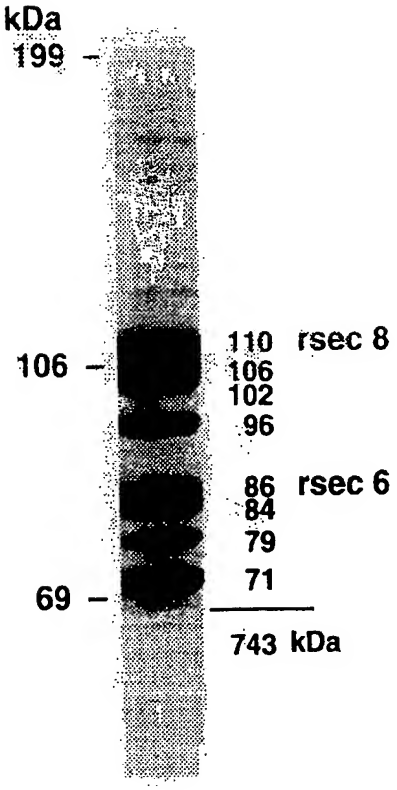
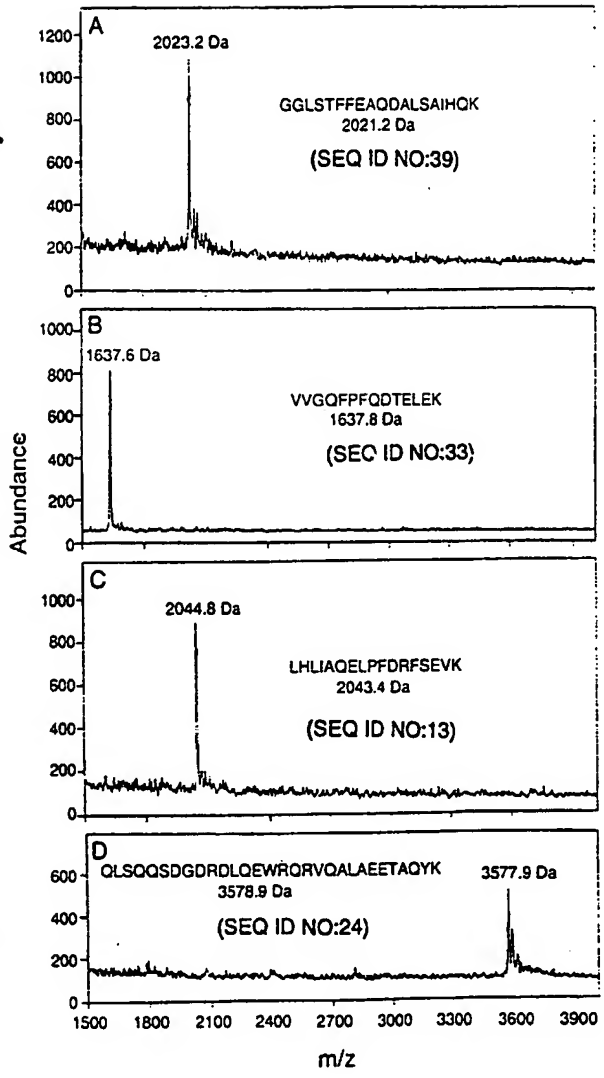


Fig. 3A

Fig. 3B

Fig. 3C

Fig. 3D



rsec8	1. XAPEGPLIDVXNI
	2. EFAAFFAK
	3. XLGVQRPLLQSTSIXE

Fig. 4A

p106	1. XXYGEIAXK
	2. XATVSLPEK
	3. XDYGVIAND
	4. LIKYFFMVASVK
	5. ELPEFNLHFFK
	6. XLQDVDLASXR
	7. XNRXNEPAVNVL
	8. XQLXNIVEPEXIY

Fig. 4B

p102	1. YLSGLQAPGXPASQSIGAQ
	2. GGLSTFFEAQDALSAIHQK
	3. ASNTADTXRQER
	4. XRENYIEGGI
	5. ENLGRLFENYI
	6. XDYDVVINDYE
	7. XIPXLSTRPANP

Fig. 4C

p96	1. VVGQFPFQDTELEK
	2. XVYEIFDN
	3. DFLESIR
	4. XDQDLQLADYDHMT
	5. STNLLLTRTLXN

Fig. 4D

Fig. 4E

rsec6
1. DFRQSINTIEXL
2. QGPSQASPNYXP
3. AAIQSQLDGVRTGLSQ

Fig. 4F

p84
1. QLSQQSDGDRDLQEWRQRVQALAEETAQYK
2. XLQLSFNFSEPNRQRP
3. SIPLALLPAAAAGA
4. DAVXQNSTQAAETEN
5. DYRNDEA
6. ENNPEEDDPS
7. XLSQQSDXG
8. AAALRAPPXVTS
9. XKREPLE

Fig. 4G

p79
1. XTDYIAE
2. ETYGAFLSRSXG
3. XXPPQGVPYNPASP
4. XXQEEETLMFIRGN
5. ALFIRDDXQF
6. NLPVFQSCL
7. AVEYFQDKFPD
8. YRVEQVGDMIDRLFDTS
9. VYEDPALSAIFLHNNYNY
10. XXYGAFLHRYSSVPFVYGXH

Fig. 4H

p71
1. XNQVAFQHFQELDEHI
2. VCHLXDQLEXVN
3. LHLIAQELPFDRFSEVK

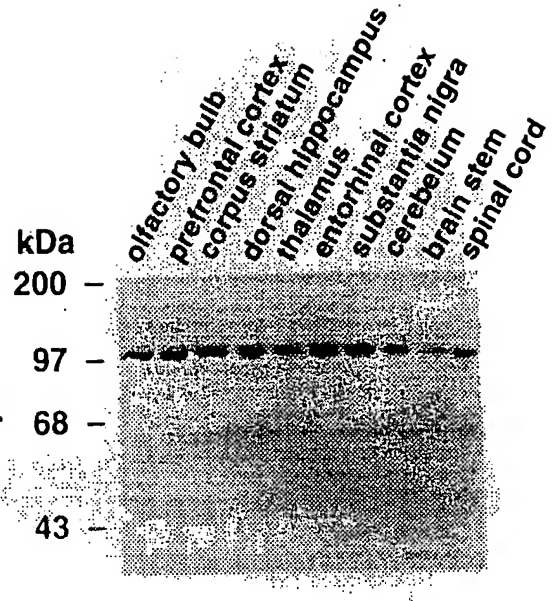

olfactory bulb
prefrontal cortex
corpus striatum
dorsal hippocampus
thalamus
entorhinal cortex
substantia nigra
cerebellum
brain stem
spinal cord
kDa
200
97
68
43

Fig. 5A

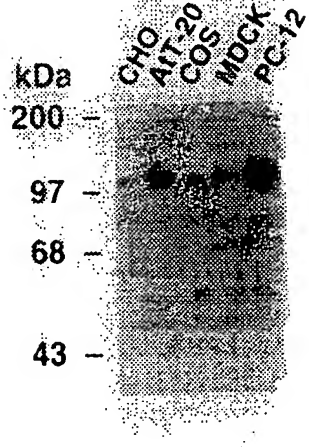

CHO
AIT-20
COS
MDCK
PC-12
kDa
200
97
68
43

Fig. 5B

Fig. 6A

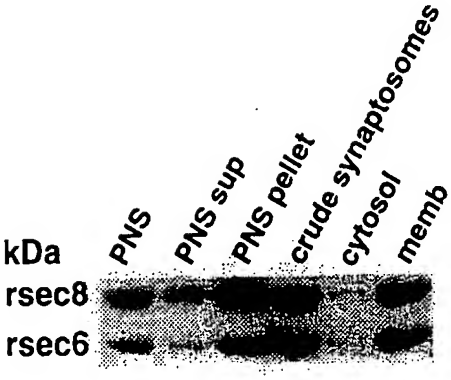


Fig. 6B

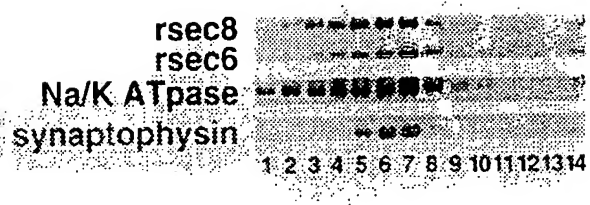


Fig. 6C

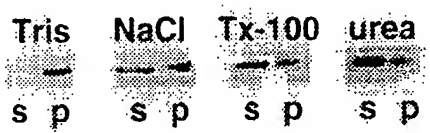


Fig. 6D

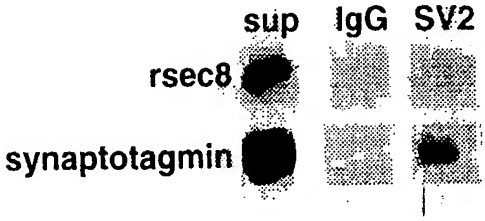


Fig. 7A

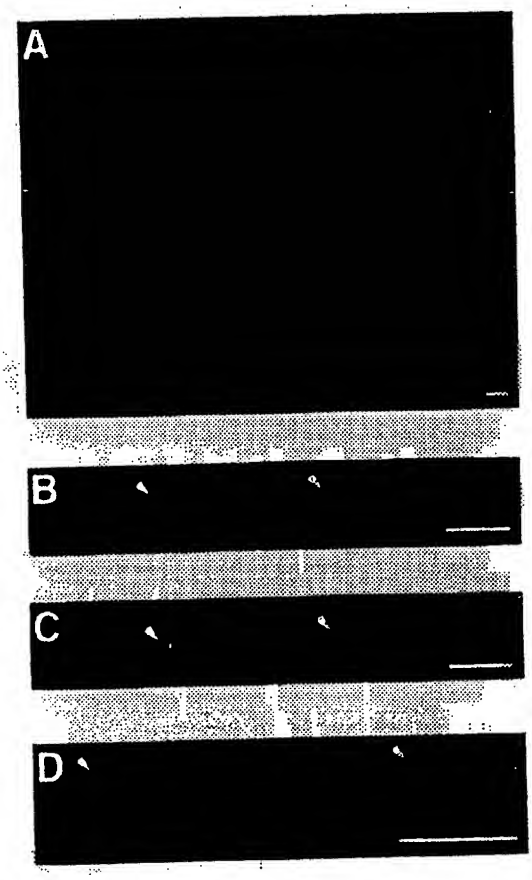


Fig. 7B

Fig. 7C

Fig. 7D

Fig. 8A

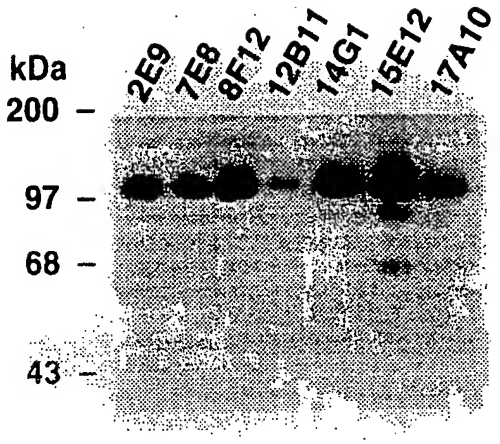
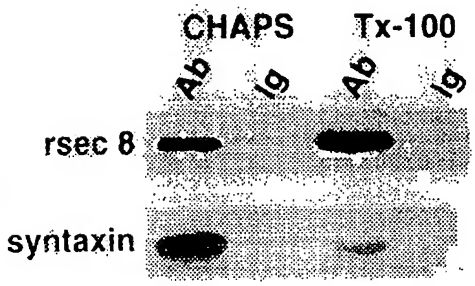

kDa
2E9
7E8
8F12
12B11
14G1
15E12
17A10
200 –
97 –
68 –
43 –

Fig. 8B


CHAPS
Tx-100
Ab
Ig
Ab
Ig
rsec 8
syntaxin